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EXPERIMENTAL STUDIES ON PORTAL CIRCULATION AT INCREASED INTRA-ABDOMINAL PRESSURE

BY

SVEN OLERUD

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BY

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MED. LIC., GÄSTR.-HÄLS.

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To my Wife

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INTRODUCTION

The purpose of this work is to discuss the importance of intra-abdominal pressure as it affects the liver and the portal circulation. The investigation has been restricted to an examination of increased intra-abdominal pressure caused by distension of the intestines, notably certain conditions arising during ileus, such as low ileus, adynamic ileus and post-operative meteorism.

The patho-physiological developments during high ileus can be explained by the large liquid and electrolyte losses which accompany these conditions and which account for both the course and seriousness of the illness.

With low ileus, during which distension of the intestines and increased intra-abdominal pressure are very often pronounced symptoms, no serious disturbances in the liquid and electrolyte balance are found. There must therefore be some other reason for the symptomatology of low ileus. It has often been suggested that toxins in the intestinal canal are responsible. It is thought that these are normally found in the intestinal canal or are formed in the distended intestinal loop during the course of the illness and in some way become absorbed and exercise a general toxic effect on the organism.

Although this has been the ruling theory for more than a hundred years, it has not been definitely proved. A symptom found in several types of ileus, and given too little consideration, is the increased intra-abdominal pressure. This work is to emphasise the unfavourable state of the liver, especially as regards its blood supply from the portal vein, during increased intra-abdominal pressure.

CHAPTER I

GENERAL SURVEY OF LITERATURE

The predominance of intra-abdominal or intra-peritoneal pressure in the free abdominal cavity is a factor of great physiological importance which influences several life functions including respiration and blood circulation. It is extremely difficult to assess exactly the value of intra-abdominal pressure, since it varies considerably according to differentiations in physical constitution, attitude and exertion, to mention a few factors only.

Normal Intra-Abdominal Pressure

In a standing position where there is a supple abdominal covering and an absence of gases and other contents in the digestive tract, the pressure just above the umbilicus corresponds to the atmospheric pressure. Below the diaphragmatic dome there is a sub-atmospheric pressure of about 10 cm water. Down towards the pelvis the pressure increases according to the laws of hydrostatics and is estimated at about 30 cm water. In the lying position abdominal pressure is distributed so that the highest degree is in the deepest parts of the abdomen. Propping (1910, 1920), in a theoretical investigation, describes the pressure circumstances in the abdomen. The estimations mentioned above are drawn from his work and correspond well with the results reported by Drye (1948) and others. Drye measured the pressure in different parts of the abdomen with the help of inserted rubber balloons. Holmdahl (1922), who among others measured the pressure under the dome of the diaphragm with a cannula inserted under the dome, found sub-atmospheric values of the same magnitude. Hörman (1905) and Emerson (1911) are among those who have investigated the degree of intra-abdominal pressure. Emerson, in a careful survey consisting of some forty essays, considers intra-abdominal pressure to be slightly positive and evenly distributed in the abdominal cavity. A neuromuscular reflex maintains the

positive intra-abdominal pressure which, however, disappears when the abdominal muscles and the diaphragm are paralysed.

Variations in abdominal pressure are caused by respiration. Most authors working on this subject confirm that inspiration causes an increase, and expiration a reduction, in the prevailing intra-abdominal pressure. Qurin (1901) points out that these conditions are changed during dyspnoea when abdominal pressure as well as the abdominal muscles must be used for expiration. During physical exertion there occurs an increased intra-abdominal pressure which reaches excessive values during, for example, Valsalva's manœuvre, when a pressure of more than 200 mm Hg has been observed (Kelling, 1903; Keith, 1923).

Increased Intra-Abdominal Pressure

Increased intra-abdominal pressure may result from a variety of conditions. Expansive processes in the abdomen, such as tumours or pregnancy, entail only a small increase of abdominal pressure since the abdominal muscles have the ability to stretch to a limited degree without causing an increase in tension. When the muscles have stretched to a maximum, a sudden increase of pressure occurs in the abdomen, a fact which has been noted during experimental investigations by a number of scientists, including Coomb (1922). Even when ascites is forming, the abdominal pressure remains low until the amount of fluid reaches an excessive degree, whereupon abdominal pressure is suddenly increased. The estimations of abdominal pressure lay between 30 and 50 cm water (Qurin, 1901, and Weitz, 1909).

Post-operative meteorism and adynamic ileus are conditions often associated with high intra-abdominal pressure. The most characteristic of these conditions are more or less paralyzed intestines and an abundance of gases in the lumen of the intestines, frequently accompanied by an irritation of the peritoneum which increases the tension in the abdominal muscles. The rise in intra-peritoneal pressure which occurs in these circumstances is easily understood, differences in physical constitution being an important factor. Thus, muscular persons have a greater tendency to high intra-abdominal pressure than, for example, women with an abdominal covering relaxed by pregnancies.

In order to gauge the influence of intra-abdominal pressure on post-operative rupture, DRYE (1948) used water-filled balloons placed in the abdomen for a week after abdominal operation. In his work DRYE mentions a case with a moderate degree of abdominal distension which showed an intra-abdominal pressure of 21 cm water measured in the median line at the umbilical level in a lying-down position, the normal value being below rather than above 5 cm water.

Ileus and Intra-Abdominal Pressure

Three different forms of ileus may be mentioned, namely, simple obstructive ileus, strangulation ileus, and adynamic ileus, though these often occur simultaneously.

The third type differs from the first two in that the motorism in the intestines is reduced and the gases in the intestinal canal are more evenly distributed. It is particularly in this case that a considerably increased abdominal pressure must be expected. The intestines are filled with gases and are paretic, and, in addition, there is often an irritation of the peritoneum with an increased passive tension in the muscles of the abdomen which in turn increases the possibility of a high intra-abdominal pressure.

This combination of ileus and high abdominal pressure has largely been disregarded in research work. WANGENSTEEN (1942) touches very briefly on that point in his detailed monograph on ileus, and so does CHESTERMAN (1945). WANGENSTEEN describes increased pressure in the ankle veins and a prolonged circulation time through the abdomen with the sodium-cyanide method. The degree of intra-abdominal pressure during ileus is not clear from the literature, but both WANGENSTEEN and CHESTERMAN point out the effect that pressure has on respiration, especially when pressure is high.

At the surgical clinic in Uppsala the intra-intestinal pressure was measured in a case of adynamic ileus following appendectomy and was found to be 40 cm water. The experiment was done in the following way: In the median line, just caudalwards of the umbilicus, an incision of about 3 cm was made through the abdominal wall to the peritoneum, through which a small hole was made. A cannula was then placed in the nearest small intestinal loop and connected with a water-manometer. Thus abdominal pressure was unchanged. There were no intestinal movements, and the gases

in the abdomen were evenly distributed, as confirmed by X-ray examination. The part of the intestine which was cannulated was not more distended than the rest of the intestines, which shows that the intra-intestinal pressure measured could be considered the same as the intra-abdominal pressure, i.e. 40 cm water.

The Origin of the Gases in the Intestines

How do intestinal gases originate during meteorism and ileus? There are three possibilities: (1) Air is swallowed down into the stomach and is conveyed onwards by the intestinal movements. According to Wangensteen and Rea (1939), this is above all caused by respiration. In trials on dogs these authors have shown that less gas accumulates during experimental ileus when the oesophagus has been tied round than when it is left intact. (2) Intestinal gases originate from the digestion of food. This process is, according to McIver (1934), especially marked during mechanical ileus. (3) Intestinal gases arise from gases which are dissolved in the blood and diffused into the lumen of the intestines. Wahren (1950) explains the factual process in the following way: Through stasis in the intestinal wall, caused among other things by ileus, the capillary vessels increase their carbon dioxide concentration, and part of this passes into the lumen of the intestines. The equilibrium between the remaining gases in the blood and intestinal lumen is disturbed owing to a change in volume. The tension of the other gases in the intestinal lumen is lessened in relation to the blood owing to an increase in volume caused by the diffusion of carbon dioxide. To restore an even balance again, the other gases in the blood (particularly nitrogen) diffuse. The carbon dioxide tension is thus again lessened, and in this way a vicious circle is produced. Wahren presumes the presence of a certain amount of swallowed air for the initiation of this mechanism, but, in my opinion, this is not necessary. The condition is simply that a gas of some sort exists or is formed in the intestine. Hibbard (1936) who points to the fact that nitrogen easily diffuses from blood, considers that at mechanical obstruction about 20% of the intestinal gases originate from the blood.

According to Hibbard (1936) the intestinal gases consist of 70% nitrogen, which shows that a balance with the nitrogen tension in the blood has not yet been obtained. 6–9% consists of carbon

dioxide, and 10–12 % of oxygen. Hydrogen and methane account for less than 1 % each, and sulphurated hydrogen for 1–10 % of the total amount of gases.

Intra-Intestinal Pressure

As a rule there is a normal pressure of 2–4 cm water in the intestine (Elman and Aird, 1935). During peristaltic movements it can become a great deal higher — 50 to 60 mm Hg (Meurling, 1952). The accumulation of gases and fluid in the intestinal lumen considerably increases the pressure. Sperling, Paine and Wangensteen (1935) reported sustained pressure readings ranging from 4–19 cm water during simple obstruction produced in dogs. The higher pressures were obtained further up in the intestinal canal owing to an active secretion there. In human beings Wangensteen (1942) found 12–54 cm water pressure during obstruction of the large bowel. Sperling, Paine and Wangensteen (1935) found during simple obstruction of the small intestine a pressure of 4–18 cm water in five different cases.

With closed loops exceptionally high pressures can be obtained, particularly if these loops are placed high up in the intestinal canal. Morton and Sullivan (1930) experimenting with dogs measured a pressure of 52 cm water in closed jejunal loops compared with 8 cm water in ileal loops. As stated above, this seems to be explained by a more active secretion in the higher part of the intestinal canal. The process of exudation must not be overlooked here.

The above-mentioned intra-intestinal pressures are in many cases exceedingly high, and it seems natural that they should interfere with the circulation through the intestines. That this is the case is pointed out by a number of scientists (van Zwalenburg, 1907; Usadel 1926; Gatch, Trusler and Ayers, 1927; Dragstedt, Lang and Millet, 1929).

Gatch and Culbertson (1935) consider that the circulation through the intestinal wall, principally in the mucosa, completely ceases at a pressure of 20 mm Hg. Sperling and Wangensteen (1935) showed that a sustained pressure of 10 cm water for 27–28 hours caused petechial haemorrhages in the intestines. It is the ante-mesenteric border of the intestine which is first affected by the impaired circulation through the intestine, and it is here that ulceration, gan-

grene and ruptures most frequently occur (Gatch and Culbertson 1935).

As will be seen from the foregoing statements, there is reason to believe that a high pressure can arise in a single intestinal loop. If the greater part of the digestive canal becomes filled with gas, the intestines enlarge and intra-abdominal pressure is of necessity increased, as in certain forms of ileus.

Intra-Abdominal Pressure and the Circulation System

(a) *The condition of the blood pressure at increased intra-abdominal pressure.*

Increased intra-abdominal pressure invariably causes a disturbance of the circulation. This disturbance can appear both locally, i.e. within the abdomen, and also generally in the form of a change in blood pressure, and possibly an altered per-minute volume caused by increased peripheral resistance.

Semb and Berg (1933) studied blood pressure readings after abdominal operations, and showed increases which varied according to the degree and duration of the meteorism. This was not the case with operations other than abdominal ones. The night pressure, i.e., the blood pressure measured two hours after the patient had fallen asleep, did not show the normal physiological decrease.

The effect of the increased intra-abdominal pressure on the blood pressure caused by experimental ascites has been the subject of much study. Several authors, including Hamburger (1896) and Thorington and Schmidt (1923), reported an increased blood pressure during an abdominal pressure of 25–30 cm water, but stated that subsequently the blood pressure fell if the abdominal pressure was raised further. Coomb (1922), however, could not confirm these findings. Instead, she found a rise in blood pressure after relief of the abdominal pressure.

(b) *The blood circulation through the abdomen at high intra-abdominal pressure.*

The resistance in the abdominal vessels strengthens with increased abdominal pressure. Great force is needed to drive the blood forward against a high pressure. By measuring the pressure in different vessels, such as the portal vein and the mesenteric veins, it is possible

to form an estimate of the resistance which the circulation must overcome. Bellis and Wangensteen (1939) determined the circulation time from the ankle to the carotid sinus, and found it to be considerably prolonged in the presence of abdominal distension (see page 11). Further, they found an increased venous pressure in the veins of the ankle. In experiments with dogs these authors showed a decreasing portal pressure as the intra-abdominal pressure rose. No change was seen in the caval vein, while in the femoral vein the pressure increase corresponded to the intra-abdominal pressure. They explained the unchanged pressure in the caval vein by the fact that this vessel was protected from the effect of the pressure by a strong fascial sheath in front of it. Jönsson (1951) showed a lengthened circulation time from leg to heart post-operatively after laparotomy, but did not correlate this with post-operative meteorism.

Ridley (1951), experimenting with rabbits, states that the pressure in the caval vein as a rule follows the intra-abdominal pressure and that it stays above the latter up to 30 cm water abdominal pressure. He obtained no exact measurements of the portal pressure, but considered that the portal pressure was higher than both the intra-abdominal pressure and the pressure in the caval vein. He secured an increased intra-abdominal pressure either by inflating the intestines with air or by merely blowing air into the abdomen.

Hoffbauer, Bollman and Grindlay (1950) studied pressure conditions in the portal vein and the abdomen of intact unanaesthetized dogs under different experimental conditions. They found that after food intake the pressure in both the portal and caval veins below the diaphragm increased, and considered this to be the outcome of increased intra-abdominal pressure.

The bloodflow of the liver during increased intra-abdominal pressure caused by a girdle round the abdomen was studied by Bradley (1946). He found that, with an outer pressure round the abdomen of 80 mm Hg, the portal bloodflow decreased in 5 out of 8 cases.

The Portal Circulation during Meteorism and Ileus

The bloodflow through a distended intestine no doubt decreases, a fact confirmed by a great many authors (see page 13). Gatch and co-workers (1927) showed that however much the pressure in an intestinal loop was increased, there always existed a small residual

circulation which probably passed via vessel communications in the mesentery. Dragstedt, Lang and Millet (1929) consider that this shunting of the blood through the intestine itself becomes so marked after a time that the venous bloodflow returns almost to the value it had before the intestine was distended. Lawson and Chumley (1940) did not note any difference, either in the arterial supply or in the venous discharge of the intestines, at a pressure of up to 30 mm Hg. The effect of distension prolonged beyond 5 minutes was not studied. Lawson and Ambrose (1941–42) found that under certain conditions the oxygen capacity of the venous blood in a distended intestinal loop was almost doubled at the above-mentioned pressure. Cocaine neutralized this effect.

Usadel (1926) showed that the portal flow was decreased to about half when, using Hürthle's flowmeter (1903), air was blown into the small intestines. This experiment was performed on only one dog and did not last longer than 4 minutes.

None of the investigators mentioned has measured the size of the bloodflow through distended intestines *when surrounded by an increased intra-abdominal pressure*, i.e., with the abdomen closed.

The volume of the portal blood at high intra-abdominal pressure caused by accumulated gas in the intestines is still an unsolved problem. The pressure in the abdomen does not only affect the blood circulation through the intestinal wall, but it must be assumed that the pressure even forms a resistance to the bloodflow in the mesenteric vein, in the portal vein and in the liver.

A number of authors, among others McMichael (1932) who worked with cats, estimate the normal pressure in the portal vein at 8–10 cm water, as measured from porta hepatis. Hoffbauer, Bollman and Grindlay (1950) found in unanaesthetized dogs an average pressure of 6 cm water in the portal vein. Wiggers, Opdyke, and Johnson (1946) give a value of 12 mm Hg for dogs. These authors measured the resistance in the liver with the help of pressure gradients and bloodflow. In the portal vein they found a resistance of 0.0174 and in the hepatic artery of 1.14. These figures are explained by the formula $R = \frac{A - V}{F}$, R being the resistance for the arterial flow and portal flow respectively, A − V the difference in pressure between the vessels on both sides of the liver, F representing the bloodflow of each vessel.

The Effects on the Liver of Increased Intra-Abdominal Pressure

This is a subject which has not received much attention, although many have investigated the relation between ileus and liver function. To what extent the increased intra-abdominal pressure influences the appraisal of these conditions is difficult to say since abdominal pressure is not as a rule included in the calculations.

Liver Function during Ileus and Post-Operative Meteorism

As regards liver function during ileus and post-operative meteorism, Werelius (1922) and Brockman (1927) considered liver deficiency to be an important factor in the pathology of ileus. These writers have not, however, put forward any convincing theory in support of this suggestion. Cole and Elman (1932) showed an increased retention of the phenoltetraiodophthalein during experimental ileus in dogs. After 10 minutes there was a retention of 21% compared with 9.8% in the control animals. Colp and Louria (1925) could not show any phenoltetrachlorphthalein retention during ileus. Seulberger (1929) showed that the amount of glycogen in the liver was quickly reduced, and that the blood-sugar sank quite quickly during experimental ileus. The glycose tolerance test showed a higher graph the longer the ileus had lasted.

Hultén (1952), who studied the prothrombin index after operations, found an increased dicumarol-sensitiveness in patients who had some sort of intestinal obstruction. This indicates a liver deficiency under such conditions.

Liver Pathology during Ileus and Post-Operative Meteorism

Cole and Elman (1932) found in dogs with experimental intestinal obstruction a central necrosis of the liver lobules in 54% of the series. The pathological change was more marked during strangulation ileus. Seulberger (1929) found, among other things, vacuole formation in the liver cells, which he considered to be an indication of fat degeneration.

Macroscopical changes in the liver during ileus with a high intra-abdominal pressure have been discovered by HULTÉN (1951). On section he found the right lobe of the liver to be darker in colour than the left, and there were more marked parenchymal changes in the right lobe. He explains this by the divided blood supply of the liver. The greater part of the blood from the small intestines and the big bowel goes to the right lobe of the liver, and during ileus this lobe is most damaged by an impaired portal bloodflow and by the bacteria and toxins which flow into it in larger quantities than into the left lobe. The oxygen in the blood of the intestines may also be reduced owing to the sluggish circulation through them during distension. On the other hand, there is the possibility that the blood from the spleen, which normally has a considerably higher oxygen content than the intestinal blood (OLERUD, 1953), reaches the left lobe of the liver without any further reduction in oxygen content. The left lobe is therefore more favourably placed during ileus. KRAMER and LUFT (1951) also point to the high oxygen content of the blood in the splenic vein, but have not correlated this finding to the oxygen content of the blood from the mesenteric veins.

Bile Secretion

The ability of the liver to form bile has often been considered a functional liver test, however crude, since the liver possesses many other functions besides the production of bile. As regards bile secretion, a great deal of research work has been done to ascertain how the bile is formed and the factors which are dependent on it.

BILE SECRETION IN RELATION TO BLOODFLOW THROUGH THE LIVER

It is generally held that the bloodflow through the liver determines the bile secretion. HEIDENHAIN found an increase in the bileflow after a splanchnic nerve section, and regarded this as a result of the increased bloodflow. The bloodflow in the mesenteric artery increases after food intake (HERRICK, ESSEX, MANN and BALDES, 1934), but KOSTER, SHAPIRO and LERNER (1936) among others did not find an increased bile secretion in this connection, which would seem to disprove this thesis.

Tanturi and Ivy (1938) increased the portal flow on dogs by irrigating the big bowel with water at 45° C, and thus increased the bile-flow. By partly clamping the portal vein a small decrease in bile-flow was obtained. When tied off completely, the bile secretion ceased altogether in a very short time. Animals entirely deprived of the portal flow by evisceration show a 50% reduction in bile-flow. Whipple and Hooper (1913) showed that animals with Eck's fistula secreted bile in much smaller quantities than the control animals did. By occlusion of the hepatic artery Tanturi and Ivy (1938) produced an increased bile-flow which they explained by the fact that the hepatic artery absorbs water from the bile as it passes the bile ducts. Engstrand (1949) found an unchanged bile secretion after occlusion of the hepatic artery, not counting an initial decrease.

BILE SECRETION IN RELATION TO THE OXYGEN SUPPLY OF THE LIVER

The experiments with occlusion of either the portal vein or the hepatic artery, mentioned in the previous paragraph, are one way in which to study the bile secretion during a decreased oxygen supply. By letting animals breathe a low percentage oxygen mixture, it has repeatedly been pointed out, a more marked anoxaemia is produced than by occlusion of one of the supplying vessels of the liver. Engstrand (1949) secured a considerable reduction of the bile-flow by this method, using 9% oxygen in nitrogen. Hanzon (1952) obtained the same result with 6% oxygen, and similar though less marked results were reported by Tanturi and Ivy (1938), and further by Glikson and Rubel (1940) and Schnedorf and Ohr (1941).

THE PRESSURE OF THE BILE SECRETION

By the bile secretion pressure is meant the pressure as measured from the level of the porta hepatis, where the secretion of the bile ceases. McMaster and Elman (1926) estimate this pressure to be about 30 cm water in dogs. Engstrand (1949), who has made a detailed study of the pressure of the bile secretion under different conditions, reported between 25.5 and 29 cm water in cats and dogs, respectively. Judging from the results of Engstrand, the pressure of the bile secretion in rabbits must be somewhat lower. The pressure decreases by about 6 cm water when the hepatic artery is occluded.

The blood pressure seems to play an important part in the maintenance of this pressure. On the other hand, neither the portal pressure nor the portal flow has any effect on the pressure of the bile secretion, if the hepatic artery is intact.

BILE SECRETION DURING ILEUS

Werelius (1922) found bile secretion to decrease during ileus and the bile to change in appearance. Schnedorf (1942) reported a decrease in bile secretion when he experimentally distended the intestines of dogs. He is of the opinion that the degree of intestinal distension and of liver function are in definite relation to each other, and he attributes this to a reflex released from the distended intestines.

Hultén (1948) showed that the size of the bile-flow was dependent upon the degree of intra-abdominal pressure, and considered a decreased bloodflow in the portal vein to be the cause of this effect.

THE TOTAL BLOODFLOW OF THE LIVER

Burton-Opitz (1911) found with the help of a flowmeter that the total flow of blood through the liver of dogs was 25 ml per kilogram of the body-weight per minute. Grab, Janssen and Rein (1929) and Grodins, Osborne, Ivy and Goldman (1941) determined with a flowmeter the bloodflow through the liver to be 25–28 ml per kilogram of body-weight. Blalock and Mason (1936) achieved the same results on unanaesthetized dogs by collecting the blood from the hepatic vein. These authors found the oxygen consumption of the liver to be on an average 0.045 ml oxygen per gram liver substance.

THE BLOODFLOW OF THE HEPATIC ARTERY IN RELATION TO THE TOTAL BLOODFLOW OF THE LIVER

Burton-Opitz (1910, 1911, and 1912) with his applied method found that the hepatic artery's part in support of the liver was 25–30 %. Working with thermo-flowmeters, Grab, Janssen and Rein (1929) determined the hepatic artery's part as being 12–22 %, while Grindlay, Herrick and Mann (1941) and Schwiegk (1932) indicate 20–22%.

Schwiegk (1932) also found that there is, under certain conditions, an indirect relation between the flow through the hepatic artery and

the portal vein. Among other things he showed that the flow through the artery increased when the portal vein was occluded. The same result was obtained by Bauer, Dale, Poulsson and Richards (1932) from *in vitro* experiments on the liver of dogs and also of Burton-Opitz (1911). Engstrand (1949) showed a 5–10% increase of the bloodflow of the portal vein when the hepatic artery was clamped.

CHAPTER II

METHODS

Animals, Anaesthetics

The animals used for the present work were exclusively rabbits. Their weight varied between 1.9 and 3.0 kilograms. Very great care was taken in the selection of animals. Too old or too fat animals were found to be too delicate for the operation. The rabbits were only allowed water 12–24 hours before the experiments.

As anaesthetic urethane was used all through the experiments. The rabbits were given a dose of 1.6 grams urethane per kilogram of their weight, in the form of a 25% or 50% solution, slowly injected into an ear vein.

In some of the experiments, especially those requiring a major operation, antishock treatment was given in the form of blood with heparin, dextran and once or twice Ringer's solution. The blood was taken from the heart of unanaesthetized rabbits.

Preparation and Technique

The animals were prepared on an operating table with heating regulation. For the bigger experiments it took about an hour to make them ready. A very careful preparation was of the utmost importance to prevent shock. During the operation the intestines were covered with compresses which were now and again washed over with warm saline solution. The animals were also kept warm by a lamp placed over the table. Oxygen (through an open mask placed over the rabbit's nose or through a canula placed in trachea) was given as a rule.

The rabbits were operated on with a long incision in the median line. After the preparation the abdomen was always closed.

The arterial blood was measured with the help of an ordinary blood pressure cannula placed in the carotid artery.

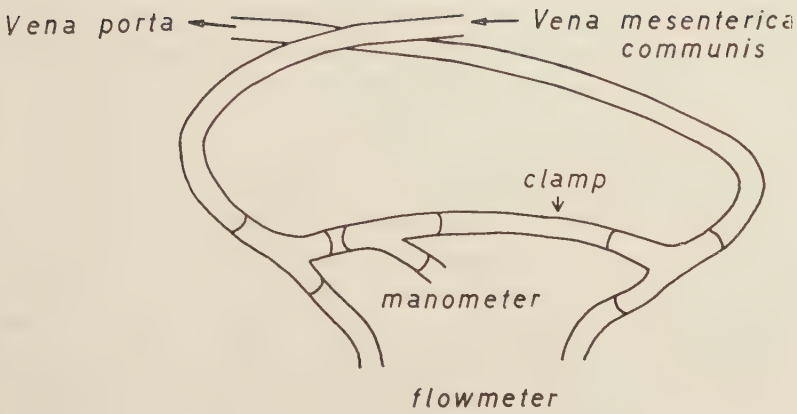


Fig. 1. The by-pass tube connection.

The blood pressure in the portal vein was as a rule measured by a polythen catheter or by a glass cannula placed in the splenic vein. These were placed so that their tips emerged in the portal vein. The supplying and emptying vessels of the spleen were as a rule ligated. One of the gastric veins which in rabbits joins the splenic vein close to the portal vein was also ligated.

The pressure in the lower caval vein was measured by a polythen catheter placed in the right jugular vein, or by a catheter in the renal vein. In the first-described method the pressure in the hepatic vein was also measured. The position of the catheter in this vessel was checked by post mortem examination.

In a number of experiments the bloodstream of the common mesenteric vein was diverted via a tube communication outside the abdomen to the portal vein (see fig. 1). This technique was used when the flow-meter was connected, and when the portal angiograms were taken (chapter IX), and also when the neoprene casts of the liver were made (chapter X). In those experiments where the role of the portal bloodflow for the bile secretion was determined, a connection with the common jugular vein was added. The widest possible tubes were used, so that the resistance in this communication should be as small as possible. As a rule the tubes had an inner diameter of 4 mm and an outer diameter of 6 mm and were made of soft plastic material. All artificial vessel tubes, cannulas and catheters were thoroughly rinsed with saline and heparin before use.

The construction of the above-mentioned bypass-tube needed a certain technique, so that the preparation itself did not form too big a trauma for the animal. And besides, it had to function properly even when the abdomen was closed and air was blown into the intestines. It was therefore important that the connecting tubes were assembled without any kinks. When the intestines were distended there was a risk that the connections to the vessels might be dislocated.

The construction of the bypass was done in the following way. Both ends of the bypass-tube were put through the right abdominal wall. The end to be connected to the central part of the portal vein was inserted just above the crista iliaca, and the end to be placed in the common mesenteric vein was inserted just below the bow of the chest. The intestines, including the duodenum, were laid over to the left so that the portal vein was exposed from behind. The splenic vein merging into the portal vein, easily seen from here, was tied. A vessel-stem approximately 2 cm long was thus freed from other connections. Ligatures were carefully placed round the portal stem to the middle and peripherally, and then the common mesenteric vein was clamped with a pair of rubberclad forceps. An incision was then made in the portal vein, and both ends of the shunt were quickly placed in the vessel and the bypass opened. All this had to be done very quickly, as the rabbit might otherwise receive a shock caused by increased pooling of blood in the intestines following the clamping of the common mesenteric vein. The tube connection was from the beginning filled with saline or blood with heparin. The shunt functioned very well, although a great many experiments had to be made before the right technique was learnt. As a rule the blood did not coagulate. During the experiments where this shunt was used the portal pressure was measured in it.

In order to collect the bile from the liver a polythen catheter was placed in the common bile duct and drawn right up to the confluence of the big bile ducts. During all these experiments the cystic duct was tied off. In some experiments the liver was screened off from the ventricle and the intestines with the help of thin knitting-needles pierced through the abdomen so that they formed a coarse trellis. Against this, compresses dipped in saline were packed to build a partition, against which the intestines rested. In this way the liver came to rest free from pressure when the intestines were inflated with air.

To develope a distension of the intestines and with that a high intra-abdominal pressure, the intestines were inflated with air. Three T-cannulas were placed at different levels in the intestines — one in the upper jejunum, one in the lower ilium, and the third one between these two. After this the abdomen was closed up, and air was slowly blown into the three cannulas. In this way air was distributed evenly in most of the intestines. This was controlled when the abdomen was opened again. In a few experiments air was blown into the intestines manually with the help of an India-rubber ball. As a rule the cannulas were connected to an air-filled bottle which was slowly filled with water under positive pressure.

What intra-abdominal pressure to use was partly determined by the condition of the experimental animal. However, the pressure was seldom raised above 40 cm water.

Apparatus, Methods of Measurement

All recording was done mechanically on a Brodie-Starling kymograph, with the exception of the registration of the oxygen capacity of the portal blood.

PRESSURE RECORDING

The arterial blood pressure was measured by a mercury manometer with a float and a writing point. The manometer was connected with the blood-pressure cannula in the carotid artery by a lead tube containing a 3.8% sodium citrate solution.

The venous pressure, the pressure of the inferior caval vein, the hepatic vein and the portal vein, was recorded with the help of the following system: a 3.8% sodium citrate solution, air, tambour and writing-lever. The base line for the portal pressure graphs has been drawn through porta hepatis and for the other pressures through the opening of the caval vein in the diaphragm. On all venous blood-pressure graphs in this work the pressure has been calibrated against a water manometer. The volume displacement of registered pressure up to 25 cm of water was 2 ml.

The aim of the investigation was not dependent on the recording of rapid variations in pressure. The present method of measuring was therefore considered satisfactory.

The intra-abdominal pressure was registered by the following method: A rubber balloon containing about 15 ml water was placed in the abdomen and was connected with a tambour by water and air. Inside the balloon was a pressure of 4 cm of water. Pressure below this volume was not measured. A volume displacement of the rubber balloon at a pressure of up to 30 cm of water was 2 ml. All the pressure graphs have been calibrated against a water manometer.

THE FLOWMETER

To measure the volume of the bloodflow has always been a delicate problem in physiology. Several methods have been developed and used with more or less success. The so-called thermo-electric flowmeter has been considered the most successful one (Rein 1927). The greatest advantage with this method is probably the fact that the bloodflow is measured bloodlessly, that is to say without the vessel having to be opened. The electro-magnetic flowmeter (Wetterer 1937, Kolin 1936) has the same advantage as the thermo-electric one.

Certain conditions must however be complied with before the above-mentioned flowmeters can work accurately. The most important of these is that the vessel in which the bloodflow is to be measured must not be subject to pulling and stretching; that the vessel keeps its configuration; and that the unit surrounding the vessel is unchanged in relation to the same the whole time during which the recording is in progress.

In the present work, where the task has been, among other things, to measure the variations of the portal bloodflow at different intra-abdominal pressures, there has been reason to assume that the portal vein changed in both configuration and position during the course of the experiments. For this reason the above methods have not been suitable.

For my tests a blood method proved to be the most suitable procedure.

Dawes, Mott, and Vane (1953) have stated a principle regarding a flowmeter which measures the volume of the bloodflow by means of a blood method. I have developed and adapted this method for my experiments.

The advantage of this new flowmeter is that the exact volume flowing through it can be measured with accuracy. The basic principle goes back to Ludwig's classical flowmeter (see fig. 2).

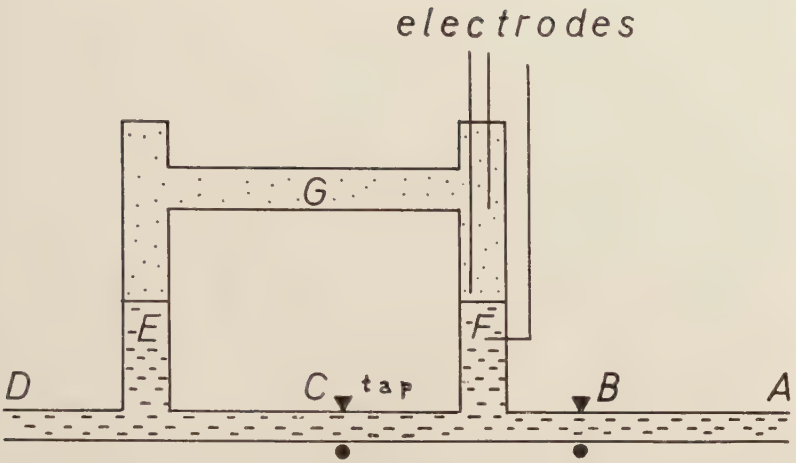


Fig. 2. An outline of the flowmeter. Dotted area silicone, chain-dotted area blood.

In the flowmeter the blood passes from A to D. G consists of an indifferent liquid. When the connection at C is closed, the blood flows up the shank F. The same amount of blood that goes up in F flows out of E. When F is filled in Ludwig's flowmeter the shanks reverse. F then empties into D and E is filled from B. With this new flowmeter the connection is opened at C when F is filled, and therefore F empties itself that way. When F empties, the flowing stops at B, and when that is finished, B is opened again and at the same time C is closed.

G is a liquid of low viscosity and a low specific gravity. It is also indifferent to blood. The system is very sensitive and the equilibrium between F and E is easily restored.

The opening and shutting of the valves at C and B is done by two electromagnets which are manœuvred by a relay which receives impulses from three electrodes immersed in F. The liquid G does not conduct electricity. Therefore an electrical circuit through the lower and higher electrodes is closed when the blood surface in F reaches the higher electrode. C is then opened and B shut. The blood column decreases in F, the middle electrode takes over the electric circuit from the higher electrode. When the blood surface in F passes the lower end of the middle electrode, the current is switched off. Then C is shut and B opened and the electric circuit has leaped over to the higher electrode to which the blood surface in F must rise so

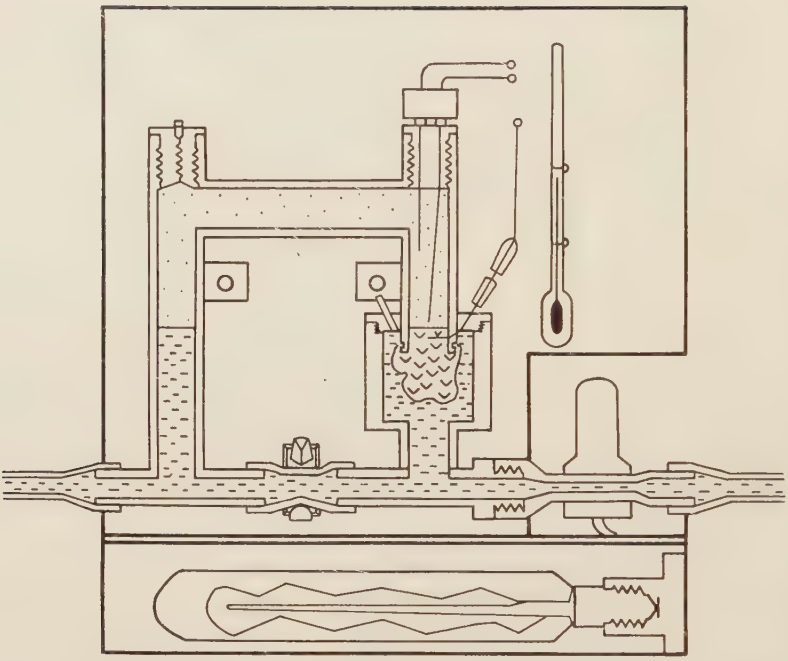


Fig. 3. The flowmeter in detail. Supplying arm to the right with oxymeter ear-unit attached to the cuvette.

that C can open and B shut again. The blood stream is thus divided into small quantities, and each quantity takes the same time to pass through the flowmeter. These time units are added electrically by a synchronous motor which mechanically registers on a kymograph. I shall revert to this in my description of the apparatus.

The Flowmeter in Detail

The flowmeter can conveniently be divided into four units, 1) the blood-conducting, 2) the mechanical, 3) the electrical, and 4) the recording unit.

A model of the blood-conducting unit is seen in fig. 3. It is made of plastic material (ICI Perspex tubes). The inner diameter of the chamber, shanks and connecting tubes is 23, 10 and 5 mm, respectively. The right shank widens at the base into a chamber. The tube that forms the higher part of this shank penetrates into the chamber and forms the neck for fixing a balloon of thin rubber. The chamber,

which is easily removed, is equipped with an air-release hole. At the top each shank is closed with a plastic screw. The left screw has a concave bottom and an air-release cock at the top. The right screw has a connecting plug which also forms the holder for two of the electrodes in the right shank. These electrodes are of different length. The distance between their tips determines the volume of the quantities into which the flowmeter divides the bloodflow. The third electrode goes sideways into the shank on a level with the top of the chamber. The electrodes are made of silver wire 0.5 mm thick.

At their base the two shanks are connected by a soft latex rubber tube with an inner diameter of 6 mm.

The rubber diaphragm in the chamber stops the blood from coming into contact with the electrodes. In spite of the minimum of current passing through them, they would otherwise soon be covered with bloodclots. The rubber balloon contains a solution of a few ml saline to form a conductor between the electrodes.

Down on the right shank is a chamber formed like a cuvette. It is fitted to an ear unit belonging to Berg's oxymeter. The inner measurements of this cuvette are 2×10 mm and the openings have a cross section of about 16 mm^2.

The Mechanical Unit

The blood-conducting unit is mounted on a metal holder. Below the tube system is a heating device, consisting of a 25 Watt lamp. This lamp is connected with a contact thermometer adjusted at 37°C. The blood-conducting unit and the lamp, that is to say the whole front of the flowmeter, is covered by a plastic sheath.

At the back of the metal holder are two magnets. They alternately open and shut two valves, one in the connecting tube between the shanks, and one in the supplying tube of the flowmeter. The arrangement of this mechanical unit is seen in fig. 3 and 4. The iron core of the magnets and the armatures are made of soft iron. Their contact surfaces are cone-shaped in order to improve the efficiency of the transmission system and to speed up the movements of the armatures at each impulse. The coils around the iron core are each wound with 4000 turns of varnished copper wire 0.3 mm thick. Each coil has a resistance of 60 Ohms. As shown in the diagram (see fig. 4), the bloodflow first passes the left magnet and flows through the cuvette with the oxymeter unit before reaching the right shank.

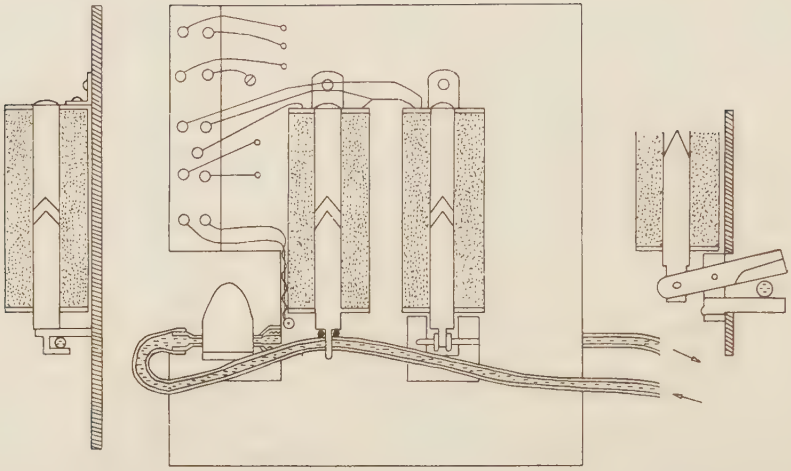


Fig. 4. The flowmeter from the back. The arrangement of the valves is seen to the left and to the right.

The Electrical Unit

The electrical unit of the flowmeter consists of an electric relay built of a transformer, a cut-off relay and a tube of the PL-21 type. Through this relay the three electrodes of the blood-conducting unit are connected with the two magnets via an additional relay R_1, a transformer and a rectifier. (See circuit diagram in fig. 5.)

In figure 5 the circuits are connected with the magnet M_1 in action. Because the grid in the tube has a negative voltage, no current passes through it. When the contact liquid (saline) in the right shank rises it closes the circuit between the electrodes C and B. Then the voltage in the tube's grid diverts positively and the current passes through it. This current closes the relay R and now 2 becomes charged and the relay R_1 closes and the magnet M_2 comes into action, and M_1 ceases to work. When the relay R closes, A takes over B's function. When the saline sinks in the right shank of the flowmeter it breaks the circuit A–C, just as it passes the electrode at the end of A. Then the grid diverts negatively and the flow through the tube ceases. The relay R is switched off and the cycle of operations returns to its first phase. The magnet M_1 functions again and M_2 ceases its action.

The time required by the blood columns in the two shanks of the flowmeter to get into balance again is nearly always constant. This time

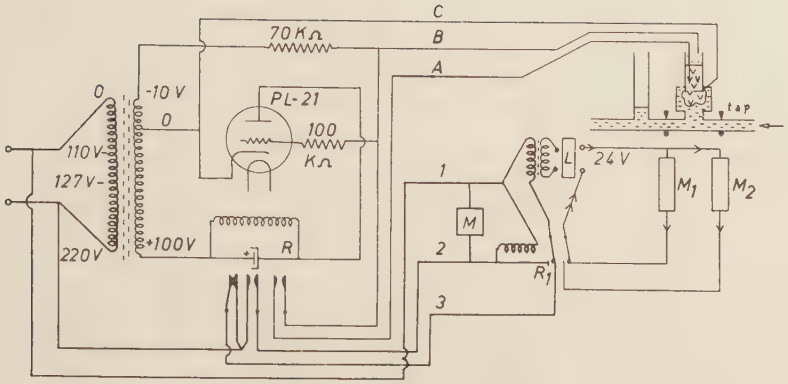


Fig. 5. Circuit diagram.

interval which equals the time in which 1 and 2 are charged (see fig. 5) is used for recording. Between 1 and 2 a synchronous motor is connected, which adds up the time intervals taken by the flowmeter to restore the balance in both shanks.

The Recording Unit

A synchronous motor with reduction gear drives a shaft on which an electromagnet and two sliding contacts are mounted (see fig. 6). The magnet is formed like an iron cylinder with the coil inside. The magnet has an armature formed like an iron disk, freely movable on the shaft. When the current is switched on, the armature is pulled against the magnet and follows the rotation of the magnet and its shaft. The magnet is driven by a low-voltage continuous current through the sliding contacts. With the help of a time-switch this current is broken for a second every half-minute. During this second an elastic returns the armature to its initial position. The edge of the armature holds a steel wire located in a slit. The wire carries the writer of a kymograph (see fig. 6). The distance the fixing point on the armature covers in half a minute is in direct relation to the deviation of the curve on the kymographic paper. The electrical impulses from the flowmeter drive the synchronous motor. The torsional moment of the motor is thus the sum of the impulses. With the help of the magnet described above, the adding up is done every 30 seconds.

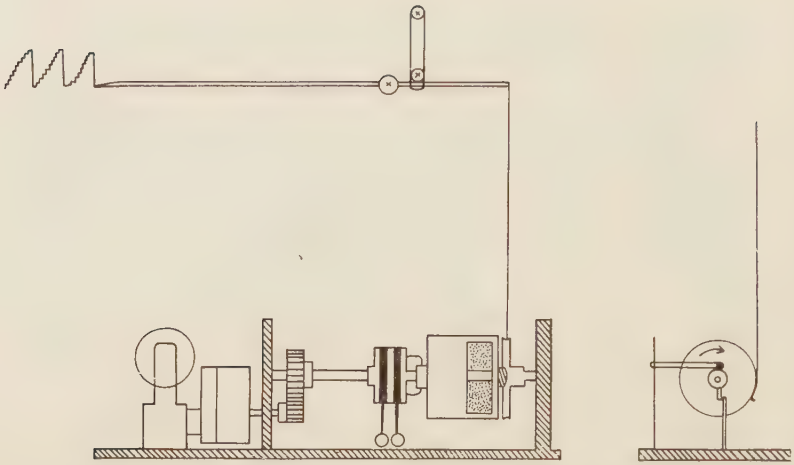


Fig. 6. The recording unit. From left to right: synchronous motor, gears, sliding contacts, magnet with the armature.

With this recording unit it has been possible to draw a chart on an ordinary kymograph in direct relation to the amount of blood that passes through the flowmeter during a certain time unit.

How to Adjust the Flowmeter for Use

First the supplying and discharging tubes are connected. Then the apparatus is wiped with silicone. Saline with a little heparin is rinsed through the flowmeter. The tubes and the apparatus halfway up the left shank are filled with blood containing a little heparin. All air is let out through the air-release hole in the chamber. The flowmeter contains about 20 ml blood altogether. About 3 ml saline is filled in the right shank above the rubber membrane. The right quantity is determined when the liquid level reaches just below the long electrode (A in fig. 5). The blood level in the left shank should be a little lower than the saline in the right shank. This is to be prefered because the rubber balloon must not be crumbled during the experiment. Lastly, the rest of the flowmeter is filled with silicone and the plastic screws tightened so that there is no air left in the apparatus. The flowmeter is now ready to be connected to the vessel in which the bloodflow is to be measured.

The silicone used in the flowmeter is of low molecular substance. The specific gravity is 0.76. It has a viscosity of 0.65 centistokes. The low viscosity makes it very useful for this purpose.

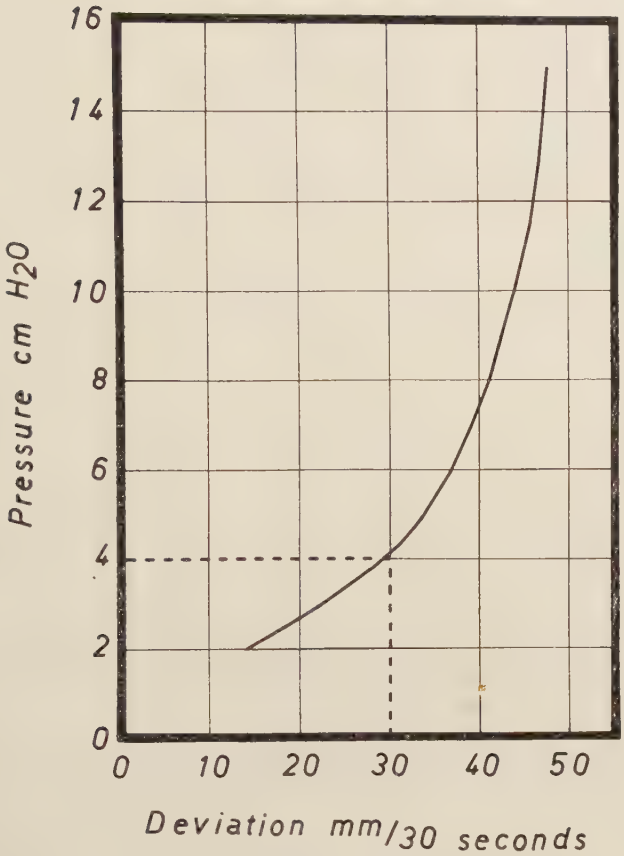


Fig. 7. Flow-resistance in relation to deviation in mm per 30 seconds.

The Flow-Resistance in the Flowmeter

Different volumes of blood per time unit were put through the flowmeter while the water column in front of it was measured. The pressure behind the flowmeter was kept constant. The relation between the resistance of the flowmeter measured in cm water and the blood that passes through it per time unit has been plotted in fig. 7. As the graph shows, the flowmeter gives quite a large resistance when larger quantities of blood pass through it per time unit. The measurings of the portal blood flow in this work seldom show volumes bigger than 30 ml per half-minute, and according to the graph the flowmeter has a resistance of less than 4 cm water at this

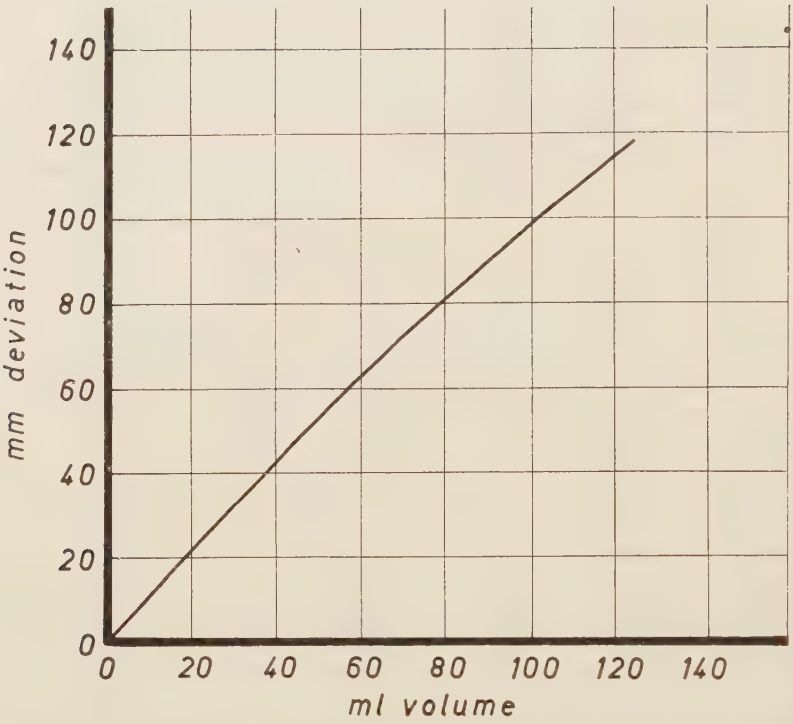


Fig. 8. The relation between the deviation in mm and the amount of blood in ml passing the flowmeter.

volume. Therefore the readings obtained with the flowmeter must be estimated as being somewhat lower than in reality. And likewise the measurements of the portal pressure are a maximum of 4 cm water too high when the flowmeter is used.

The Capacity of the Flowmeter. The Volume per Half-Minute in Relation to the Deviation on the Kymograph

With the help of a pressure bottle worked under different pressures, blood has been passed through the flowmeter. The amount of blood passing through it has been found constant per time unit at the same pressure. These different volumes are measured in ml and corresponding deviations are measured in mm on the graph. It has thus been possible to obtain a basis for comparison between them. A relation between the deviation in mm and the amount of blood that has passed through the flowmeter is shown in fig. 8. The mathe-

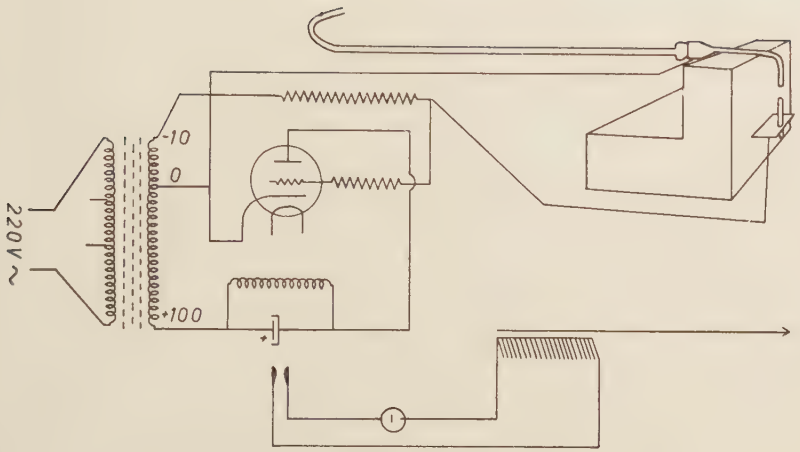


Fig. 9. The arrangement for recording bile-flow.

matical relation between the volume per time unit and the deviation varies between 0.77 for extremely low volumes and 1.15 for extremely high volumes. For a volume of 30 ml per half-minute, the ratio is 1.00 and for a volume of 20 ml it is 0.94. On the whole a deviation of 1 mm corresponds to 1 ml.

The graph on fig. 8 is drawn in the following way: The deviations for three half-minutes are added together and plotted as ordinates. The volume is marked out as abscissas and is the volume that passes through the flowmeter during 1.5 minutes.

THE REGISTRATION OF THE BILE-FLOW

The bile-flow was registered according to the drop-contact method. The arrangement is seen in fig. 9. The bile drops were formed on the tip of a cannula, and when they reached the bottom point of the tip they dropped off the cannula. In this way the drops were always of the same size. At the moment when they reached the metal point an electric circuit was closed which, through an electric relay, worked a magnet lever on the kymograph.

The Graphs of the Experiments

A standardized system for the reproduction of the experimental graphs has been used. These do not include the preparation of the animal, which to some extent explains the low arterial blood pressure

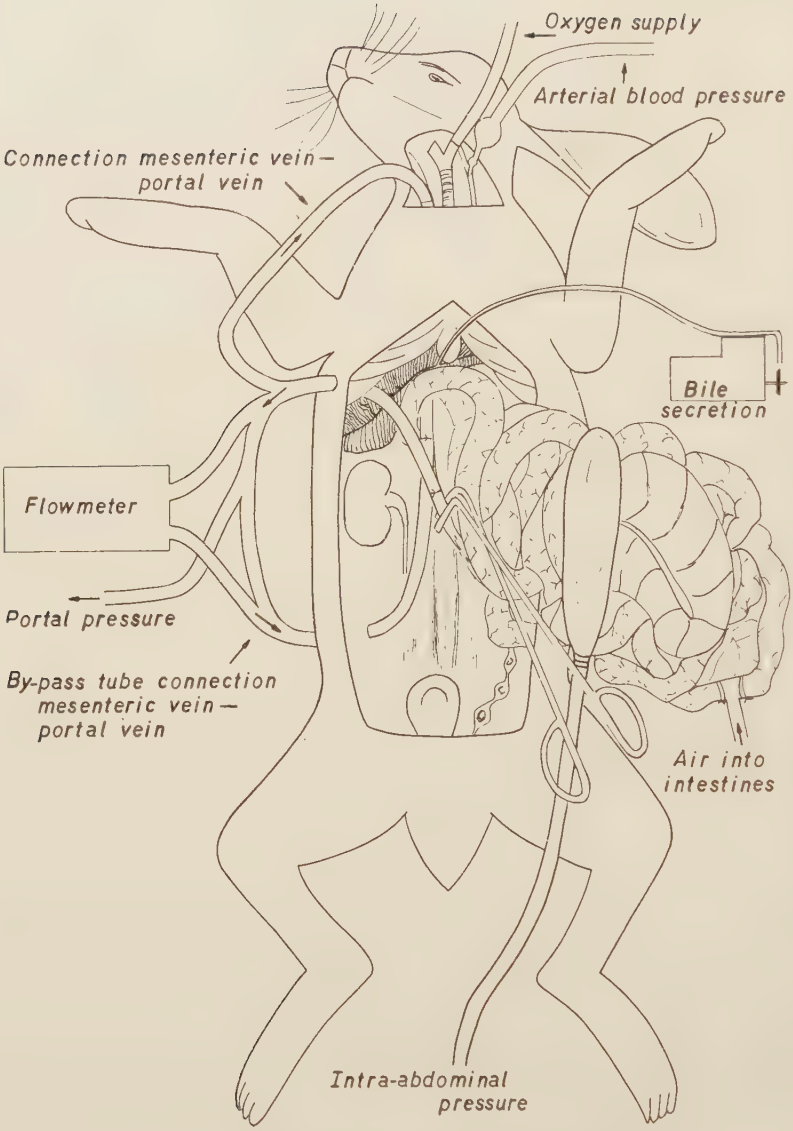


Fig. 10. General scheme of the experimental arrangement.

at the beginning of the graphs. As a rule the amount of fluid which was given to prevent shock has not been marked. It has in no experiment exceeded 40 cc fluid (blood or dextran).

The blood pressure graphs and the intra-abdominal pressure graphs state the mean pressure per minute.

The bile-flow is stated in drops per minute. More rapid changes of the bile secretion have not been considered necessary to record in these experiments.

The bloodflow through the portal vein only consists of the blood from the intestines, for the splenic circulation is cut off. The bloodflow on the graphs states the deviation of the flowmeter in mm per minute. The volume in ml per minute of the blood passing through the flowmeter is practically always the same as is the deviation of the flowmeter in mm on the graphs. Therefore, it has been considered sufficient to write ml instead of mm on the reproduced graphs (see fig. 8).

CHAPTER III

BILE SECRETION IN RELATION TO ARTERIAL BLOOD PRESSURE AND THE BLOODFLOW IN THE PORTAL VEIN

In order to determine the influence of increased intra-abdominal pressure on bile secretion, the effect of blood pressure on it must first be studied, as blood pressure may be affected by alterations in intra-abdominal pressure. Since the bloodflow often varies in relation to intra-abdominal pressure, the degree of bile secretion in relation to the portal flow must also be considered.

It is a well-known fact that bile secretion is to a great extent dependent on intra-hepatic vascular pressure, as stated by TANTURY and IVY (1938), ENGSTRAND (1949), and others. TANTURY and IVY doubt whether filtration pressure has any influence on the formation of bile, but they point out that the bile flow decreased in volume the longer the experiments were continued, a fact which my own experience confirms. This decrease may be caused either by a slowly falling blood pressure or by a reduction in the resorption of the bile salts. As all the bile is drained away during the experiment, a shortage of bile salts in the intestines will be the result.

Bile Secretion in Relation to Blood Pressure

As the fall in blood pressure resulting from these experiments is mainly due to shock, the investigation may be more aptly termed "bile secretion in relation to shock". The hypotensive conditions present during abdominal distension are also an expression of shock. Thus the investigations described in this and the following chapter can easily be correlated.

Results:

These are best shown in Figs. 11 and 12. The graphs are representative of about ten experiments. At the arrow in Fig. 11 the intestines

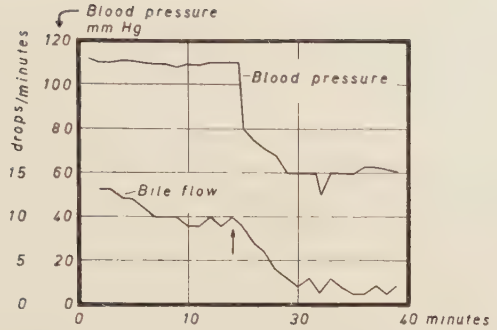


Fig. 11. Bile secretion in relation to blood pressure. At the arrow the intestines were maltreated for 10 min.

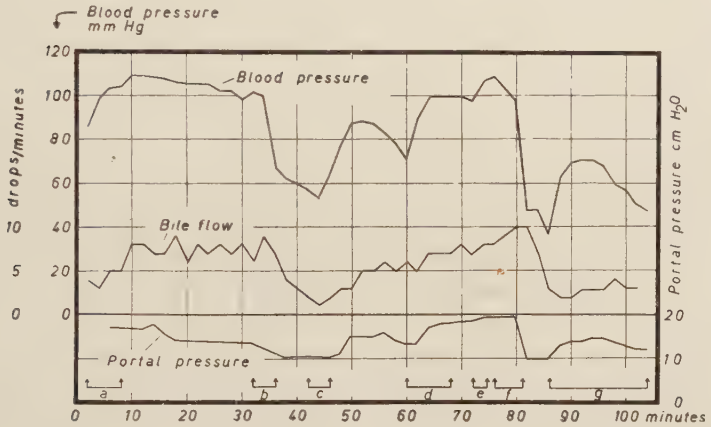


Fig. 12. Bile secretion in relation to blood pressure. a) infusion of 25 ml dextran, b) arterial bleeding 28 ml, c) infusion of 28 ml blood, d) infusion of 25 ml dextran, e) infusion of 15 ml dextran, f) arterial bleeding 37 ml, g) infusion of 37 ml blood.

were maltreated for about ten minutes. The animal undergoing the experiment was apparently very shock-sensitive, for the blood pressure fell rapidly. The bile secretion decreased from 10 drops to 3 drops per minute, simultaneously with the appearance of the hypotensive conditions.

The experiment illustrated in Fig. 12 (in which the portal pressure is also registered) shows the level of bile secretion during hypotensive conditions caused by arterial bleeding. When the arterial blood pressure was restored to normal by infusion of the withdrawn blood plus 6% dextran in saline solution, the bile secretion returned to its

previous level. The portal pressure, which is determined partly by the bloodflow from the splanchnic area and partly by the resistance in the liver, seems to follow the arterial blood pressure in its variations, but also shows a tendency to increase during the course of the experiment. This is in accordance with the statement of Wiggers et al. (1946) that there is an increased liver resistance to the portal blood during and after shock.

Bile Secretion in Relation to Portal Flow

In addition to the 'by-pass' tube connection in the portal vein, a further connection with the right jugular vein was arranged in this experiment, thus making it possible either to maintain a normal portal circulation or to break it off suddenly and lead the blood to the jugular vein. In this way the liver could be deprived of portal blood without any change in blood pressure.

In the first experiment of this type the flowmeter was connected to the by-pass tube in order to register the amount of bile-flow in relation to the bloodflow in the liver. It was easy to regulate this with the help of the shunt to the jugular vein, though this procedure was later found to be unnecessary (compare Results, below).

Results:

As seen in Fig. 13, the bile secretion was unchanged even when all the portal blood was led through the jugular vein past the liver. In the latter part of the 15-minute period during which the portal blood was led past the liver, the bile secretion, strangely enough, showed a slight increase. This can perhaps be explained by a reduction in the size of the bile drops caused by a changed surface tension. It is possible that the chemical composition of the bile changed when the portal blood was led past the liver.

When the shunt to the jugular vein was closed, a considerable fall in blood pressure resulted, from which the animal did not recover spontaneously.

Discussion:

The mechanism of bile production is obscure, though many of the factors which influence the bile are known. What most scientists have been occupied with here is the question of bile secretion in rela-

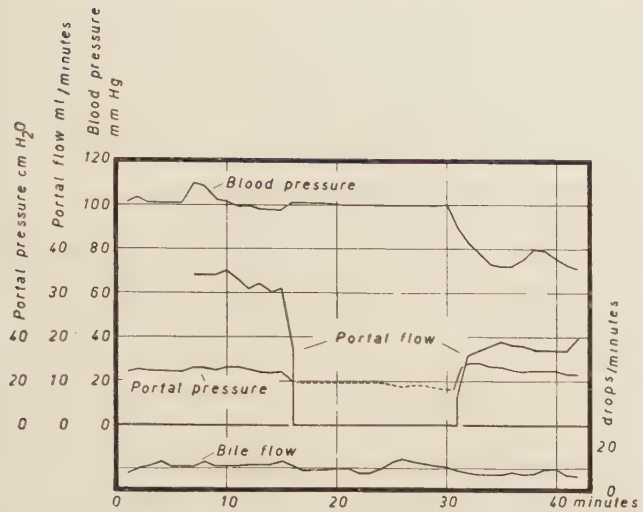


Fig. 13. Bile secretion in relation to portal flow. Dotted line shows time during which the portal flow was led past the liver.

tion to the oxygen and blood supply of the liver. When the hepatic artery is clamped, there is a reduction in oxygen supply but not in bile secretion (Tanturi and Ivy, 1938). On the other hand, a number of authors (see page 19) have found a reduction in bile secretion when the animal is subjected to hypoxaemia, either by giving it mixtures containing a low percentage of oxygen or by rebreathing (Tanturi and Ivy, 1938). In the former case the blood pressure is reduced, while in the latter there is a rise in blood pressure with carbon dioxide retention.

These are facts which the above-mentioned authors have not taken into full consideration in examining the relation of bile secretion to hypoxaemia. On the other hand, judging from the results submitted, the blood pressure seems to be an important factor in the maintenance of bile secretion.

The portal bloodflow represents 80% of the total bloodflow to the liver (Grindlay, Herrick, and Mann, 1941). Blalock and Levy (1937) showed that during haemorrhagic shock and shock caused by intestinal trauma in dogs the total bloodflow of the liver was reduced by 48% and 29%, respectively, with a blood pressure between 75 and 85 mm Hg. The liver should thus get more blood during a state of shock than when the portal bloodflow is led past the liver. Accord-

ing to this argument the blood pressure must be an important factor in the maintenance of bile secretion.

That bile secretion is maintained in spite of all the portal blood being led past the liver must indicate that the hepatic artery — at least during short periods — must supply the liver with blood and oxygen sufficient for that purpose.

The importance of bile salts in the formation of bile is not excluded by leading the portal blood to the jugular vein. The liver may be supplied with these salts by the hepatic artery. On the other hand, the capacity (blood volume per time unit) of the hepatic artery is only one-fifth of that of the portal blood. Therefore, it should take some time for the bile salt concentration in the blood to become high enough to equal the amount of bile salts delivered, per time unit, to the liver when the portal vein is intact. But even during the first few minutes the bile secretion did not show any decrease when the portal blood was led to the jugular vein. This suggests either that the portal blood has a surplus of bile salts and that the liver is dependent on only a small part of it, or else that the liver has a certain reserve of these salts which it can use until the concentration of bile salts in the hepatic artery is increased.

The reduction in blood pressure observed when the portal blood was again led to the liver can be explained in several different ways. The most probable explanation is that the sudden increase in resistance to the portal blood causes a pooling of blood in the splanchnic area, where the amount of blood drawn from the circulation may have been considerable.

Summary:

The arterial blood pressure seems to be an important factor in the maintenance of bile secretion. The bile decreases considerably during hypotensive periods, and increases to nearly the original value when the blood pressure returns to normal. During an impaired hepatic arterial bloodflow the amount of bile secretion seems to be quite independent of the portal venous bloodflow. Here one must assume that bile salts and other important substances necessary for the formation of bile and usually found in the portal vein, are being supplied to the liver via the hepatic artery.

As will be seen from the third experiment described in this chapter, the reduced bile secretion found in the first two experiments can

hardly have been caused by a reduced portal bloodflow. The fact that the bile secretion is independent of the portal flow is of conclusive importance in estimating the relation of bile secretion to increased intra-abdominal pressure caused by distended intestines, a case in which a reduced portal flow is often found (See Chapter VI).

CHAPTER IV

BLOOD PRESSURE AND BILE SECRETION IN RELATION TO INTRA-ABDOMINAL PRESSURE

Intra-Abdominal Pressure and Blood Pressure

It may be assumed that a high intra-abdominal pressure possibly reacts on the circulatory system. As stated in the Survey of Literature, a number of authors have tackled this problem and have found that the circulatory system sometimes reacts with a rise in blood pressure and sometimes with a reduction, to some extent depending on what degree of pressure has been applied to the abdomen.

To a great extent my work touches on the problems pertaining to this subject. In the following experiments an account is given of the relation of blood pressure to a slowly increasing abdominal pressure.

Results:

Fig. 14 shows the typical course of the arterial blood pressure when the intestines are distended with air at a closed abdomen.

During moderately increased abdominal pressure a slight reduction in blood pressure was noted, followed by an increase commensurate with the abdominal pressure up to a certain level. When the abdominal pressure reached about 25 cm water, there was a severe fall in blood pressure. Most of the rabbits reacted in this way to increased abdominal pressure, although several animals never showed any rise in blood pressure.

Fig. 15 (see page 47) depicts a similar experiment. In this case the blood pressure was about 10 mm Hg higher than in the former experiment. A blood pressure fall was not registered until the abdominal pressure had reached 35 cm water. This shows the importance of the blood pressure in maintaining the circulation during high intra-abdominal pressure. The higher the blood pressure, the higher the intra-abdominal pressure that can be sustained without a collapse of the circulation.

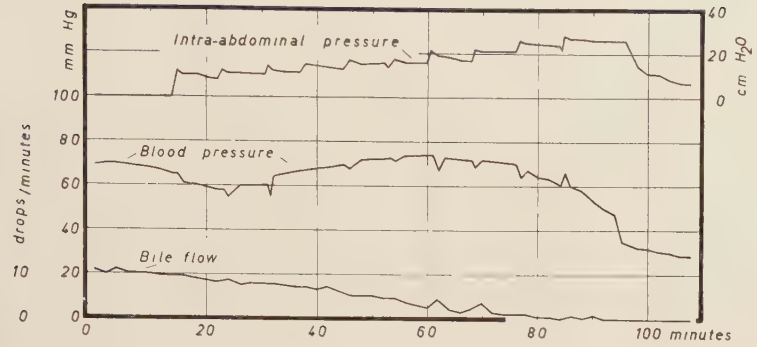


Fig. 14. Blood pressure and bile secretion during increasing intra-abdominal pressure.

Discussion:

The initial blood pressure reduction is probably the outcome of a neuro-vascular reflex caused by air distending the intestines. The low abdominal pressure existing during these hypotensive periods can hardly interfere mechanically with the blood circulation in the capillary area of the intestines or in the big veins in the abdomen.

What is the cause of this increase in blood pressure? There are several possible explanations. The increased peripheral resistance in the vessel path which results from pressure on the vessels in the abdomen may induce the heart to react with increased energy, accompanied by an increase in blood pressure.

Another possibility is that the venous depots which are to be found in the abdomen, in the liver and in the larger venous vessels, empty passively following the increased pressure. In this way the animals get an auto-transfusion of appreciable dimensions. In human beings the bigger venous stems in the abdomen contain about a pint of blood (Gatch, 1950), i.e., about one-tenth of the whole amount of blood. That a rise in blood pressure does not occur in every rabbit can possibly be explained by the fact that the rabbit lapses into a state of irreversible shock which is not affected by blood transfusions of any kind.

Burton-Opitz (1914) considers that there is a changed distribution of the blood to the various parts of the body at a high intra-abdominal pressure. In experiments on dogs, when air was blown into the abdominal cavity to reach a pressure of up to 20 mm Hg, Burton-Opitz found that the bloodflow in the carotid artery was

doubled. He believes this rise in blood pressure to be due to a mechanism similar to that arising when the aorta is compressed.

The reduction in blood pressure occurring at a pressure of between 25 and 35 cm water has been the subject of much discussion. HEINRICIUS (1890) considered this reduction to be caused by a respiratory insufficiency arising during too high intra-abdominal pressures. HAMBURGER (1896) and EMERSON (1911), on the other hand, considered it to result from a circulatory collapse caused by a reduced flow-back to the heart from the abdomen.

Summary:

The blood pressure, except for an initial reduction, increased as soon as the intra-abdominal pressure was raised. This was due either to an increased peripheral resistance or to an addition in the amount of blood already circulating, caused by a depletion of the venous depots through increasing intra-abdominal pressure. When the latter reached a value of between 30 and 35 cm water, circulatory collapse occurred with a quickly falling blood pressure. In order to avoid a collapse of the circulation during high intra-abdominal pressure it was important to maintain a high blood pressure.

Bile Secretion and Increased Intra-Abdominal Pressure

The amount of bile secretion varied with the blood pressure, which in turn was dependent on the degree of intra-abdominal pressure. An expression for the relationship between bile secretion and abdominal pressure is therefore difficult to find. Except for variations in blood pressure, it has been possible to show in several experiments a definite relationship between bile secretion and abdominal pressure. This relationship was more marked in those cases in which the blood pressure was kept constant during the course of the experiment.

Results:

The effect of intra-abdominal pressure on bile secretion is shown in Fig. 15. The secretion remains almost unchanged until abdominal pressure reaches about 20 cm water. At this level there is a considerable reduction in the secretion which ceases almost completely when the intra-abdominal pressure reaches 25 cm water. The bile secretion is reduced at a lower pressure level than is required to produce a fall in blood pressure.

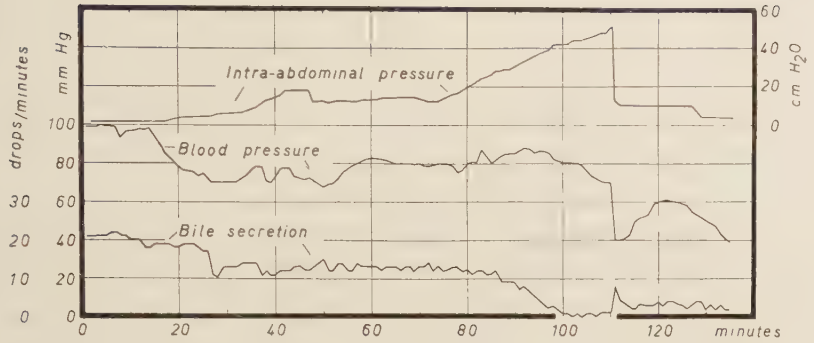


Fig. 15. Bile secretion in relation to increasing intra-abdominal pressure.

Discussion:

As the bile secretion is independent of the portal flow, a reduction in the secretion cannot be caused by a reduced portal flow resulting from a distension of the intestines. As a rule, a fall in blood pressure did not occur until the abdominal pressure had reached 25–35 cm water, but on the other hand the bile secretion was reduced at a somewhat lower abdominal pressure.

Bile secretion takes place with a certain secretion pressure which in rabbits seldom rises above 25 cm water. If the liver is subjected to a higher pressure than this, there is a risk that the secretion may cease completely as the liver is considered compressible. It is therefore possible for the bile ducts inside the liver to be compressed or for the individual liver cells to be directly prevented from producing bile.

On the other hand, SCHNEDORF (1942) held that a reflex from the distended intestine could cause a reduced bile secretion; but this possibility was ruled out by an experiment in which I protected the liver from pressure by a dividing wall placed just below it. As shown in Fig. 22 (see page 58), the bile secretion was completely unchanged in relation to the abdominal pressure. This experiment also proved the effect of intra-abdominal pressure on the liver, as accounting for a reduction in bile secretion.

Summary:

The amount of bile secreted during increased intra-abdominal pressure was found to be dependent on the pressure exercised on the liver. When the abdominal pressure was higher than the pressure of the bile secretion, the latter ceased; when the liver was relieved of pressure the bile secretion returned to normal.

CHAPTER V

PRESSURE CONDITIONS IN THE VEINS OF THE ABDOMEN AT INCREASING INTRA-ABDOMINAL PRESSURE

As the veins have very thin walls, pressure acting outside them will interfere with the pressure inside them. One might assume that as soon as the pressure outside exceeds the pressure inside, the vein will collapse owing to the lower vein pressure. Such is not the case, however, provided no collaterals pass near where the vein is subjected to pressure. Duffield and Harris (1934) showed that by constricting the limb in which the venous pressure was recorded, the venous pressure increased to the level of the arterial blood pressure. The same conditions must prevail if the portal vein or the caval vein is clamped and there are no collaterals through which the pressure can be relieved. The following experiment shows the correctness of this assumption.

Pressure in the Portal Vein when it is tied off

The by-pass tube was mounted in the portal vein, the end leading into the liver was clamped, and portal pressure and arterial blood pressure were recorded.

Result:

As shown in Fig. 16, a marked increase in the portal vein pressure was noted. The blood pressure sank considerably owing to a decreased flow-back to the heart and to pooling of blood in the splanchnic area. Both pressure graphs (representing blood pressure and portal pressure) approach each other until they register the same pressure. When the portal pressure is at its highest, it registers 72 cm water. The arterial blood pressure then shows a level of 53 mm Hg. Both these pressures correspond with each other.

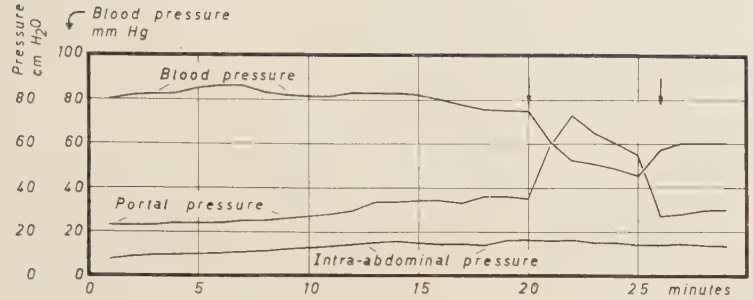


Fig. 16. Fall in blood pressure and rise in portal pressure when the portal vein is tied off. First arrow shows where the portal vein is clamped, second where it is opened.

After this, both pressures fall, the portal pressure a little faster than the blood pressure, which may be due to a few collateral vessels having opened.

Discussion:

When there is a total block in the portal vein, the arterial blood pressure will work with all its force against the obstruction so long as no collaterals develop. During this obstruction in the portal vein, the arterial pressure will be transmitted over the capillaries in the intestinal area. If there is no counter-pressure these vessels will either dilate to a maximum or else burst with a consequent extravasation of blood. With increased intra-abdominal pressure accompanied by increased pressure in the portal vein, this tendency is to some extent lessened.

Pressure in the Portal Vein and in the Inferior Caval Vein at High Intra-Abdominal Pressure

It is obvious that a high intra-abdominal pressure has a tendency to press together the thin-walled vessels in the abdomen. According to the experiment mentioned in the previous paragraph, the venous pressure overcomes all resistance so long as this does not exceed the prevailing arterial blood pressure. Therefore one may expect the pressures in the caval and portal veins to follow, on the whole, the intra-abdominal pressure.

The experiment illustrated in Fig. 17 shows that this is actually the case. In addition to the pressure in the portal vein, the pressure in

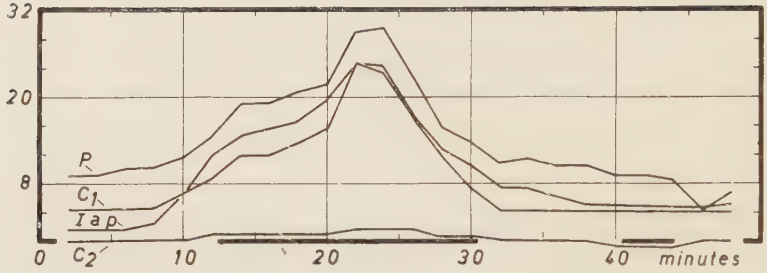


Fig. 17. Portal and caval pressures in relation to increased intra-abdominal pressure. P: Portal pressure, I a p: intra-abdominal pressure, C_1 and C_2: pressures in inferior caval vein 2 cm above and 2 cm below the diaphragm respectively.

the caval vein was recorded, both 1–2 cm above the diaphragm and 1–2 cm below it. The positions of the recording catheters were controlled after the experiments.

Results:

As the experiments show, the pressure in the systemic veins of the abdomen (in the portal vein and in the caval vein below the diaphragm) is dependent upon the height of the intra-abdominal pressure. The marked difference in the caval vein above and below the diaphragm points to the fact that the abdomen can be considered as one unit whenever intra-abdominal pressure is concerned. In this experiment at least the pressure seemed to be quite evenly distributed throughout the whole abdomen.

Pressures in the Intra-Hepatic Veins in Relation to Intra-Abdominal Pressure

(a) *Determination of the pressure in an intra-hepatic portal vessel.* This experiment was carried out to investigate whether and to what extent the abdominal pressure compressed the extra-hepatic portal stem. If it did, an increased difference would be found in the pressures of the portal vein inside the liver and outside.

Results:

As will be seen from Fig. 18, the difference in pressure between the extra-and intra-hepatic portal pressure is nearly always constant

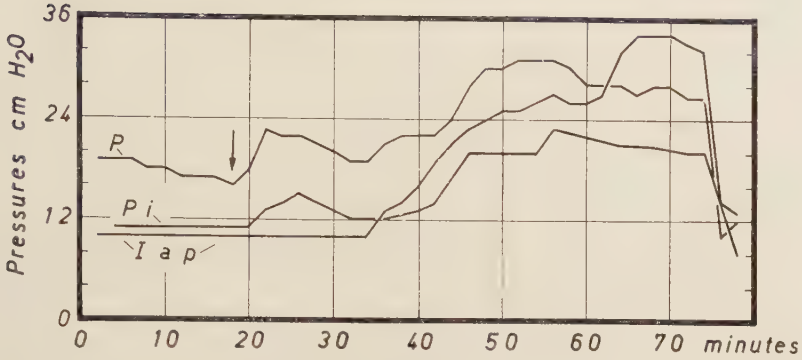


Fig. 18. The pressure of an intra-hepatic branch of the portal vein in relation to increased intra-abdominal pressure. P: Pressure in the portal vein, P i: pressure in an intra-hepatic branch of the portal vein. I a p: intra-abdominal pressure. Arrow marks where rabbit received a small infusion of dextran.

when the intra-abdominal pressure rises. On the other hand, the result indicates that there is an obstruction to the blood discharge from the liver caused by incrased intra-abdominal pressure.

One may be inclined to think that this obstruction is formed by the liver itself when subjected to increased abdominal pressure. To determine this point the following experiment was performed.

(b) *Determination of the pressure in a branch of the hepatic vein at increased intra-abdominal pressure.*

A catheter was threaded via the jugular vein through the heart to the hepatic vein. The position of the catheter was controlled after the experiment.

Results:

As will be seen from Fig. 19, the pressure in the hepatic vein followed the intra-abdominal pressure in the same way as it did in the other veins of the abdomen. Thus, the intra-abdominal pressure affected even the disharge from the liver. This can be explained by the fact that the outlet of the hepatic vein into the caval vein is placed below the diaphragm in rabbits. The intra-abdominal pressure is active on the vessels as far up as the diaphragm.

With these results it was possible to say whether the resistance in the liver was increased by a raised intra-abdominal pressure or not.

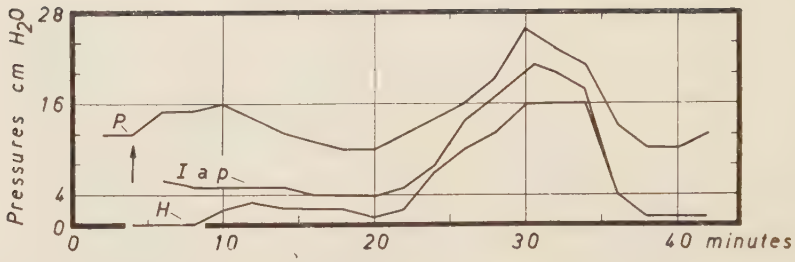


Fig. 19. The pressure in an intra-hepatic branch of the hepatic vein in relation to increased intra-abdominal pressure. P: Pressure in the portal vein, I a p: intra-abdominal pressure, H: pressure in an intra-hepatic branch of the hepatic vein. Arrow marks where rabbit received a small infusion of dextran.

Pressure in a Mesenteric Vein in Relation to Increased Intra-Abdominal Pressure

This experiment was undertaken to form an idea of the size of the pressure gradient needed to drive the blood from a mesenteric vein to the portal vein during increased intra-abdominal pressure.

A polythen catheter was placed in a mesenteric vein, and the portal pressure was recorded by a cannula threaded through the splenic vein. The pressure in the caval vein was recorded by a catheter placed in the renal vein and drawn up to the upper part of the abdomen.

Result:

As seen in the experiment illustrated in Fig. 20, the difference of pressure between the mesenteric vein and the portal vein increased with rising abdominal pressure and was more than double at an intra-abdominal pressure of 30 cm water.

This experiment also shows that under certain conditions there can be different pressures within the abdomen. The low pressures in the portal and caval veins confirm this. They also indicate that the venous pressure can rise considerably with a local pressure increase in the abdomen.

Summary:

An evenly distributed increase in intra-abdominal pressure led to an increased pressure in all the veins of the abdomen. The pressure in these was maintained by the arterial blood pressure. Even the intra-hepatic pressure, both on the portal side and on the hepatic venous

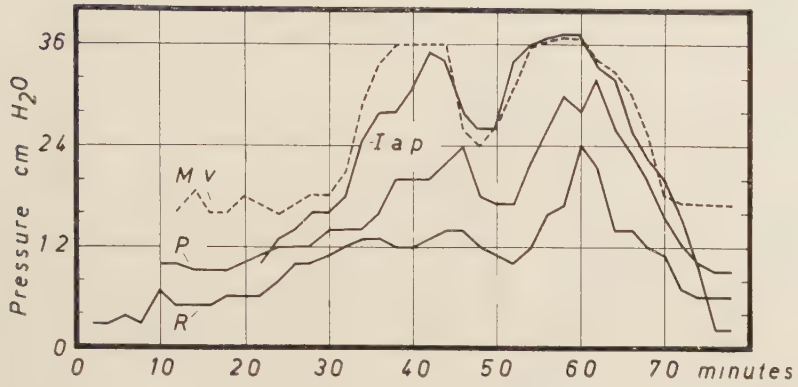


Fig. 20. Pressure in a mesenteric vein in relation to increased intra-abdominal pressure. M v: The pressure in a mesenteric vein, I a p: intra-abdominal pressure, P: pressure in the portal vein, R: pressure in the caval vein just below the diaphragm. The intra-abdominal pressure is raised twice.

side, was influenced by the intra-abdominal pressure. A local pressure increase can be found in the abdomen, with a resulting pressure increase in a mesenteric vein in those cases where the collaterals also are subjected to pressure or are missing.

Distribution of Intra-Abdominal Pressure

As described on page 26, the abdominal pressure was measured with a balloon placed in the abdomen ventrally in the median line and on a level with the umbilicus. Therefore, the pressure recorded merely represents a limited area of the abdomen. As is seen in all experiments described in this chapter, the simultaneous recording of the pressures in several veins of the abdomen shows that the increased intra-abdominal pressure due to distended intestines is quite evenly distributed over the whole abdomen.

On the other hand, there are some cases, though rather rare ones, in which the pressure is not active in the upper parts of the abdomen. In these experiments the portal pressure does not show the usual rise when the abdominal pressure is increased.

CHAPTER VI

THE EFFECT OF INCREASED INTRA-ABDOMINAL PRESSURE ON THE PORTAL BLOODFLOW

As stated in the previous chapter, the pressure in the veins of the abdomen increases to such a degree that only a certain part of the blood circulation is maintained. Studying only the pressures in the veins and the relation between these pressures, no idea of the size of the bloodflow can possibly be obtained. The pressure gradients in the respective vessels give no clue as to the size of the bloodflow, for a large pressure gradient can mean either a powerful bloodflow in widened vessels with small resistance or a small flow in compressed vessels with great resistance.

The bloodflow to the liver can be measured in different ways, either by means of a flowmeter or else by assessing the ability of the liver to absorb a chemical substance introduced into the blood, e.g. bromsulfalein. I have found the latter method less suitable. By the time all preparations for the experiment are finished, the condition of the rabbit is such that a great many unknown factors can play an important part in the metabolism of the bromsulfalein in the liver.

Of the different flowmeter methods, I have preferred that described by Dawes et al. (1953), which I have adapted for my experiments. The thermo-flowmeter method was not considered suitable, for here the position of the registered unit around the portal vein has to be completely unchanged, and this could not be counted on during distension of the intestines. This new method allows of a full record of the amount of blood passing through the flowmeter.

The flowmeter was connected to the by-pass tube (whose connection to the portal vein is described on page 23). In addition to the portal flow, a record was made of the portal pressure, the arterial blood pressure, the oxygen saturation of the portal blood, and in some cases also of the bile secretion, air being blown into the intestines as previously described.

Three types of experiments will here be discussed:

(1) The portal flow during a high and comparatively evenly distributed abdominal pressure.

(2) The portal flow during an increased intra-abdominal pressure when the liver has been relieved of pressure.

(3) The liver as a factor of resistance to the portal blood during increased intra-abdominal pressure. The resistance of the hepatic vein is also included here.

(1) The Portal Flow during High and Evenly Distributed Abdominal Pressure

An increased portal pressure in connection with an increased intra-abdominal pressure indicates a raised resistance to the bloodflow through the liver. This resistance is a mechanical result of the increased intra-abdominal pressure, as the portal pressure is not increased if the liver is protected from the influence of pressure (compare (2) below). An increased intra-abdominal pressure therefore suggests that the intra-abdominal pressure is active even in the upper parts of the abdomen, i.e., below the diaphragm.

If the degree of portal and abdominal pressure correspond, the pressure in the abdomen may be said to be evenly distributed. A possible decrease in the portal bloodflow accompanied by increased intra-abdominal pressure suggests rising resistance in the whole splanchnic area from the arterial side as far as to the inflow of the caval vein to the thoracic cavity.

Results:

A typical graph of the course of the experiment is set forth in Fig. 21. The portal flow increases slightly during the first few minutes as air is blown into the intestines. This increase is possibly caused by blood being pressed out of the capillary area in the intestines and partly out of the venous vessels in the mesentery. Then the portal flow decreases as the intra-abdominal pressure increases, until at about 30 cm water it ceases almost completely.

When the abdomen is relieved of pressure by the air being let out of the intestines, the portal flow increases and at the end of the experiment shows about half its initial value. The low portal bloodflow after the air has been let out of the intestines can be explained

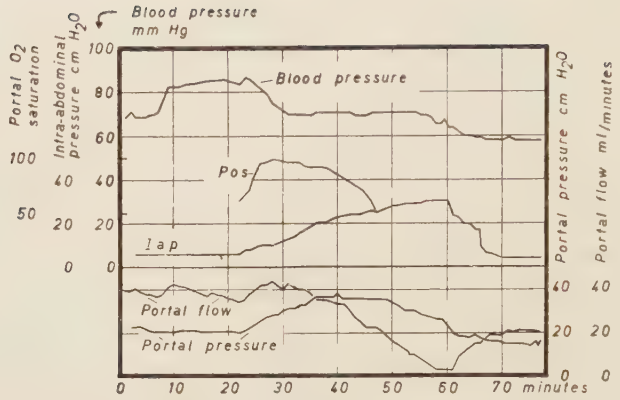


Fig. 21. Portal flow during increasing intra-abdominal pressure. Iap: intra-abdominal pressure. Pos: Portal oxygen saturation.

partly by the low blood pressure which the animal has at the end of the experiment, and partly by the fact that it is not possible to remove all the air from the intestines. Some of the intestinal loops still have an increased intra-intestinal pressure owing to kinks in them.

The table on page 57 shows values from nineteen experiments carried out in full accordance with the method described above. With an intra-abdominal pressure of 25 to 39 cm water the portal flow was reduced with 70—93 % i.e., 30—7 % of the portal flow at the beginning of the experiment.

The experiment depicted in Fig. 24 may, perhaps, show more clearly the effect of intra-abdominal pressure on the portal circulation. Instead of letting the air out of the intestines only, the abdomen was opened, thus entirely eliminating the effect of the intra-abdominal pressure. In spite of the low blood pressure, the increase in the portal flow was marked. When the abdomen was opened and the intestines were free to expand further, the intra-intestinal pressure was also reduced and the circulation in the mucosa of the intestine was thus eased.

During some of the experiments the reduction in the portal flow began almost immediately after the air was blown into the intestines, and in others first at a pressure of about 15–20 cm water. It is therefore difficult to say exactly at what pressure the reduction in the portal bloodflow begins.

Before Increase of Intra-Abdominal Pressure				Abdominal Pressure initiating Portal Flow Reduction	During Increased Intra-Abdominal Pressure				
Experiment No.	Blood Pressure mm Hg	Portal Pressure cm water	Portal Flow ml/min	cm water	Intra-Abdominal Pressure cm water	Blood Pressure mm Hg	Portal Pressure cm water	Portal Flow ml/min	Portal Flow Reduction %
313	70	20	67	10	35	60	21	6	91
317	60	20	40	10	27	50	32	8	80
318	85	20	40	20	30	65	26	6	85
322	90	16	50	8	28	75	32	8	84
323	80	30	30	8	25	70	25	5	83
324	90	30	35	12	26	80	35	6	83
325	83	22	47	20	36	90	42	14	70
368	82	23	54	10	34	55	37	4	93
369	80	18	28	—	32	55	34	2	93
370	70	22	50	19	29	30	25	6	88
371	60	23	46	17	36	60	28	6	87
372	70	23	38	10	36	70	28	4	93
373	70	18	40	9	28	60	25	6	85
374	85	20	42	27	38	50	33	10	88
375	90	20	40	12	31	50	28	4	90
376	90	23	34	6	26	40	26	6	82
377	90	18	36	25	39	65	34	6	86
378	95	22	44	14	27	70	26	6	87
379	70	20	60	7	32	60	28	14	78
					Mean 31.4				Mean 85.0

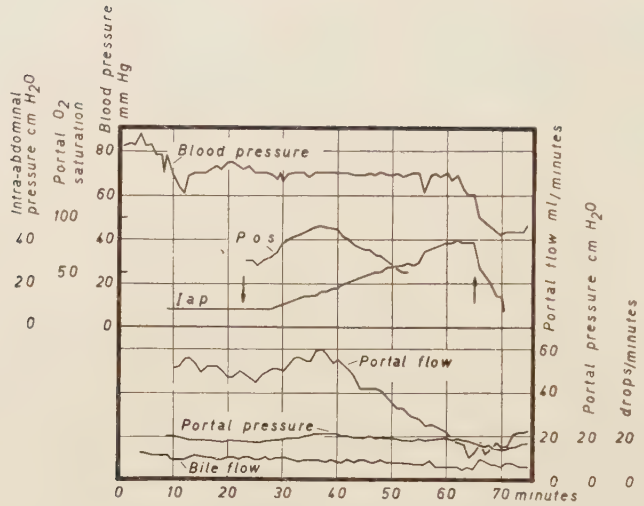


Fig. 22. Portal flow during increasing intra-abdominal pressure when the liver is relieved of pressure. Iap: intra-abdominal pressure. Pos: Portal oxygen saturation. Left arrow marks when air was blown into intestines, right when abdominal pressure was relieved. *Note.* Bile secretion unchanged in relation to intra-abdominal pressure and portal flow.

(2) The Portal Flow during Increased Intra-Abdominal Pressure when the Liver is Relieved of Pressure

In this type of experiment, which is illustrated in Fig. 22, the liver was protected from pressure by a dividing wall placed just below it. The reduction in the portal bloodflow is here caused only by the distension of the intestines and by the effect of the intra-abdominal pressure on the circulation in the vessels of the intestines and the veins of the mesentery. In addition, the degree of bile secretion is recorded in this experiment.

Results:

In all experiments (about ten) in which the liver was protected from pressure by a dividing wall, the portal pressure was fairly constant during an increased intra-abdominal pressure. In several cases a minor decrease in pressure was noted.

The results confirm the mechanical effect of the pressure rather than a contraction of the portal tree due to reflex from the distended intestine, with increased portal pressure as a result.

The experiment (Fig. 22) shows the portal pressure to be independent of the intra-abdominal pressure when the latter is not active under the diaphragm.

The portal flow does not show the same marked reduction as it did in the previous experiment carried out with a corresponding pressure. During an abdominal pressure of 30 cm water there was a reduction in portal flow of about 35 %, while with a pressure of 39 cm water the reduction was 62 %. This strongly suggests that the portal bloodflow meets considerable resistance either in the liver or in the venous pathway on the heart side of the liver sinusoids when the intra-abdominal pressure affects the liver below the diaphragm. The following experiment shows that this is the case.

(3) The Liver as a Factor of Resistance for the Portal Blood Stream during Increased Abdominal Pressure

In this experiment a connection was made between the by-pass tube and the jugular vein. When the abdominal pressure had reached a height of 24 cm water, the connection to the liver was clamped and the portal blood was then led to the jugular vein. In this way the liver resistance to the portal blood stream was removed.

In the resistance of the liver must be included also that of the hepatic bloodflow which may likewise increase owing to the raised intra-abdominal pressure.

Results: (See Fig. 23).

The portal bloodflow was, as usual, reduced during the increased intra-abdominal pressure. When that pressure reached a height of 24 cm water and the connection to the jugular vein was opened, there was a powerful increase of the portal bloodflow. This shows that a liver exposed to a raised abdominal pressure will have a considerable resistance to the portal blood stream. The initial increase can be explained by the fact that a great many venous vessels in the abdomen emptied during the decreased resistance in the portal bloodflow. During an abdominal pressure of 24 cm water the portal flow increased from 33 to 57 % of the bloodflow in the beginning of the experiment owing to its being shunted over to the jugular vein. These figures do not include the initial increase in the portal bloodflow.

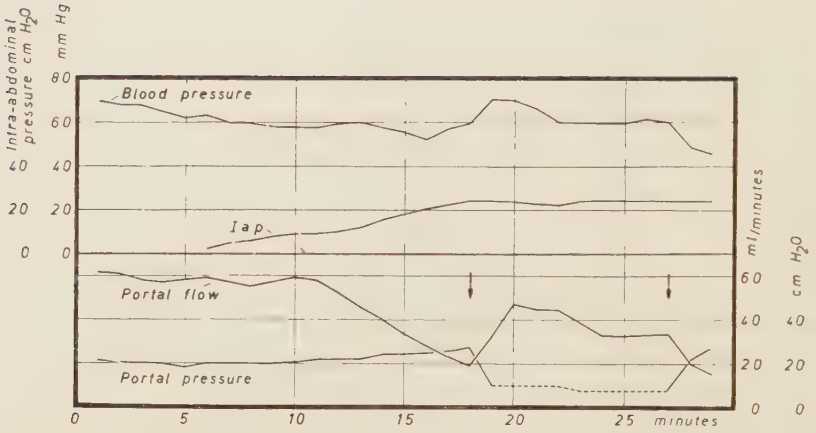


Fig. 23. The importance of the liver resistance for the portal blood steam at increased intra-abdominal pressure. Iap: Intra-abdominal pressure. Arrows mark when portal blood was led past the liver to the jugular vein.

Discussion:

The total effect of distended intestines and intra-abdominal pressure on the circulation through the abdomen is, according to the experiments shown above, quite considerable. The venous bloodflow meets an increased resistance all the way from the capillary area of the intestines to its flow-out from the abdomen, while with regard to the intestine itself it has been shown by several scientists that distension reduces the circulation through its wall. There are those who consider that the greater part of the blood flowing to a distended intestinal loop is shunted after a while past the capillary area. Thus, the reduction in bloodflow in the veins from a distended intestine should not be particularly marked (Dragstedt, Lang and Millet 1929; Lawson and Ambrose, 1941–42).

On the other hand, the difference between open and closed abdomen must here be pointed out. None of the above-mentioned authors has studied the bloodflow when the abdomen is closed. With a closed abdomen the intra-abdominal pressure affects even the serous side of the intestine, and further the vessels in the mesentery, the portal vein, the liver itself, and the caval vein. The resistance in the portal circulation becomes active in several places at the same time; in other words, the whole venous tree increases its resistance, causing an increased reduction in the bloodflow in the splanchnic area when the abdomen is closed.

Summary:

The size of the portal circulation largely depends on the degree of intra-abdominal pressure in association with intestinal distension. This pressure causes increased circulatory resistance to the venous bloodflow in the whole splanchnic area. The resistance does not only originate in the distended intestinal wall, but also in the discharging pathways of the intestinal blood and in the liver. At an abdominal pressure of between 25 and 39 cm water a reduction of 70–93 % was obtained in my experiments; i.e., 37–7 % of the initial portal flow.

CHAPTER VII

THE OXYGEN SATURATION OF THE PORTAL BLOOD IN RELATION TO INTRA-ABDOMINAL PRESSURE

The present investigation is merely a *relative* measurement of the oxygen saturation of the portal blood as it is affected by intra-abdominal pressure. The variations in oxygen saturation were measured with MILLIKAN's (1942) type of photoelectric oxymeter, the commercial Berg model B2, with a scale marked from 50 to 100, being used.

At the beginning of the experiments the galvanometer of the oxymeter was set at 60. The photoelectric cell unit was attached to a cuvette-like shoulder which was connected to the flowmeter (See Fig. 3). The inner measurements of the cuvette were 2×10 mm, there being a 3 mm slit on both sides through which the light passed to the photocell. In this way only the variations of the oxygen saturation in the central parts of the bloodflow were measured.

Results:

The effect of the increased intra-abdominal pressure on the oxygen saturation of the portal blood varied considerably. In some experiments there was a very marked increase in the saturation, with quite slight distension of the intestines and a relatively low intra-abdominal pressure (see Figs. 21 and 22).

In the experiment illustrated in Fig. 21 the oxymeter showed an increase on the scale from 60 at a normal pressure to 98 at a pressure of 12 cm water, i.e., 66 %. With a further increase in abdominal pressure the oxymeter sank slowly, and at a pressure of 24 cm water returned to 60. After this the oxymeter sank further as the abdominal pressure rose. In about ten other experiments similar changes, more or less marked, were observed in the oxygen saturation of the portal blood.

In some further ten experiments carried out in exactly the same way as those just described, the oxygen saturation of the portal

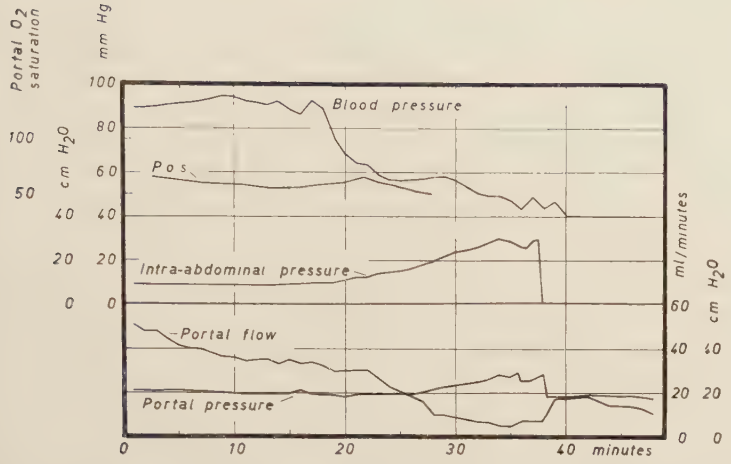


Fig. 24. Experiment showing absence of rise in portal oxygen saturation during increasing intra-abdominal pressure. Pos: portal oxygen saturation. Intra-abdominal pressure was relieved by merely opening the abdomen, air still remaining in the intestines.

blood showed little tendency to increase. In some of the experiments the intestines were inflated with oxygen and in others with nitrogen, different gases being used in order to ascertain to what extent the absorption of the gases in the intestines accounted for the results obtained. The experiments showed exclusively a reduction in the oxygen saturation as the intra-abdominal pressure increased. For an illustration of these experiments see Figure 24.

Discussion:

The increased oxygen saturation of the portal blood can be explained theoretically in this way: when the intestine is subjected to distension, blood no longer passes through the capillary area of the mucosa, but is shunted over the arterio-venous anatomosis straight to the veins. In rabbits the intestines are equipped with a large number of these anastomoses, both in the mucosa and in the submucosa (Spanner, 1931 & 1932). Lawson and Ambrose (1941–42) showed a reduced arterio-venous oxygen difference with a distended intestine, i.e., increased oxygen saturation in the blood, but this was not the case when the mucosa of the intestines was treated with 1 % cocaine hydrochloride solution.

Lawson and Ambrose, who sometimes distended intestines with

water and sometimes with a condom balloon placed within the lumen, stated that there are low-resistant shunts in the intestines which short-circuit the blood when the intestines are distended. Cocaine, on the other hand, prevents the shunts from opening.

Judging by the results of these experiments, the intestinal distension seems in some cases to be able to open the arterio-venous shunts. In other cases some unknown factor intervenes in the mechanism of the shunts and they remain closed.

On the whole, the regulating mechanism of the shunts is an unknown factor. It has not been possible to ascertain the reasons why my experiments affected the opening and closing of the shunts, and I have therefore had to leave it at that for the time being.

One might be tempted to assume that the capacity of the intestine to absorb the oxygen in the air in some cases led to an increase in the oxygen saturation of the blood, but in the experiments in which only oxygen was blown into the intestines, no increase of oxygen saturation resulted, which disproves such a theory.

The increased oxygen saturation in most cases coincided with a small increase in the portal bloodflow Fig. 22. No such increase occurred when there was no increase in the oxygen saturation of the portal blood. It is therefore possible that the shunts are in a better position to let blood through the intestinal wall than are the capillaries. This would in part contradict the earlier theory that the increased intra-abdominal pressure emptied some of the venous depots in the splanchnic area; but one theory does not exclude the other.

The increase in the oxygen saturation of the portal blood was reduced quite quickly with the decreasing portal bloodflow. The arterio-venous shunts are not sufficient to maintain the portal bloodflow or its oxygen saturation during increasing abdominal pressure. When this reaches a certain height, the shunts are possibly affected and become compressed. Moreover, the intra-abdominal pressure forms too strong a resistance for the portal bloodflow to be maintained in the peripheral veins of the arterio-venous shunts. The reduced oxygen saturation of the portal blood is due to the slackened flow through the intestinal capillaries and to the inferior function of the arterio-venous shunts, together with a greater exploitation of the oxygen in the blood.

Summary:

In a number of experiments carried out during a moderate distension of the intestines and with a closed abdomen, there was an increased oxygen saturation in the portal blood. In several experiments this was not the case. The presence of arterio-venous shunts in the intestinal wall may quite possibly explain the first results. What regulates the shunts is unknown at present, and it is an open question why they should function in some cases and not in others.

The increase in the oxygen saturation of the portal blood observed in some experiments was nearly 70 % at a moderate abdominal pressure (15–25 cm water). After that, with increasing pressure, there was a continuous reduction in the oxygen saturation, which sank below the initial values.

CHAPTER VIII

THE BLOODFLOW IN THE INFERIOR CAVAL VEIN, ABOVE THE DIAPHRAGM, DURING INCREASED INTRA-ABDOMINAL PRESSURE

According to the experiments explained in Chapter VI, the portal bloodflow is considerably reduced at an increased intra-abdominal pressure. In order to estimate the extent to which that pressure reacts on the flow-back to the heart, the size of the bloodflow in the inferior caval vein above the diaphragm was determined with the help of the flowmeter. This bloodflow contained blood from the hepatic vein, the renal vein, and the posterior parts of the body.

Method:

The rabbit was intubated through an incision in the trachea, and respiration was effected by means of a Starling respiration pump. The foremost part of the chest was removed, and the by-pass tube was placed in the caval vein, in the same way as it was placed in the portal vein in earlier experiments. The inferior caval vein above the diaphragm is about 3 cm long, and the insertion of the by-pass tube did not present much difficulty.

Results: (See Fig. 25).

When the intra-abdominal pressure was increased to 25 cm water, the bloodflow increased by 13 % per minute. A corresponding, though less marked, increase resulted when determining the size of the portal flow (compare Figs. 21 and 22 in Chapter VI).

The increase in the oxygen saturation coincided with the increase in the bloodflow. During higher abdominal pressures, the flow in the caval vein was greatly reduced, and at a pressure of 36 cm water it was 63 % of the flow at a normal intra-abdominal pressure.

The association between an increased pressure in the caval vein and an increased bloodflow can be explained partly by the greater

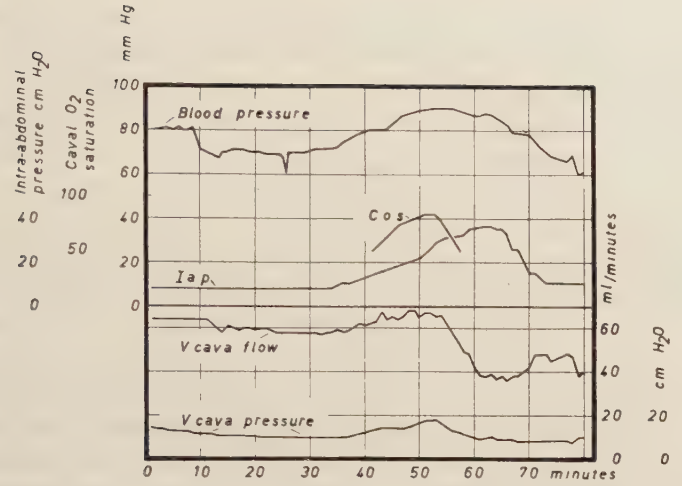


Fig. 25. Bloodflow in inferior caval vein above the diaphragm during increasing intra-abdominal pressure. I a p: intra-abdominal pressure. C o s: caval oxygen saturation. The values after 20 and 62 min. are taken as a basis for the calculations in the text.

resistance shown by the flowmeter when larger quantities of blood passed through it.

Discussion:

The relation between the rise in arterial blood pressure and in intra-abdominal pressure is seen clearly in this experiment. The blood pressure fell as soon as the bloodflow in the caval vein was reduced. On the other hand, the reduction in the portal flow could be quite considerable before this reduction was seen in a decreased blood pressure. (Compare Chapter VI Figs. 21 and 22.) It is possible that the reduced portal flow is compensated over the hepatic artery. This "delayed" fall in blood pressure suggests that the splanchnicus blood circulation is influenced by the intra-abdominal pressure to a greater extent than is the remaining circulation below the diaphragm. This is in fact quite probable because the venous system in the splanchnicus area is considerably "longer" than is for example the venous pathway for the renal blood which is likewise affected by intra-abdominal pressure. It should be pointed out here that the splanchnicus area has two capillary systems, with the intestines influenced primarily by the intra-intestinal pressure, and the liver by the intra-abdominal pressure.

The flow in the caval vein, reduced with 37 % of its normal value at an abdominal pressure of 36 cm water — compared with an 80 % reduction of the portal flow at the same abdominal pressure — in reality showed quite a moderate reduction. This supports the theory that the splanchnicus area is influenced by an increased intra-abdominal pressure to a considerably higher degree than is the remaining circulation below the diaphragm.

As stated earlier, the bloodflow from the kidneys, from the posterior parts of the body, from the hepatic artery, and from the portal vein was included in the bloodflow of the caval vein. In dogs the hepatic artery and portal vein are responsible for nearly 44 % of the total flow through the thoracic part of the inferior caval vein (Blalock and Levy, 1937). The bloodflow in the inferior caval vein is about 65 % of the total bloodflow to the heart. (Blalock and Levy, 1937.) If this figure is taken as a basis, the bloodflow to the heart in this experiment should be 91.0 ml per minute, and the reduction in the total bloodflow to the heart caused by increased intra-abdominal pressure should be about 24 %. These calculations require a normal blood distribution between the upper and lower parts of the body in spite of increased intra-abdominal pressure.

As the bloodflow to the right half of the heart is so much reduced, it is quite natural that the blood pressure cannot be maintained. An increased intra-abdominal pressure can thus be said to cause an insufficiency in the circulation.

Summary:

Judging by the results from this experiment, high intra-abdominal pressures cause a considerable decrease of the bloodflow in the caval vein above the diaphragm. The reduction of the portal flow seems to be larger than the reduction of the remaining blood circulation below the diaphragm at the same pressure. As long as there is no change in the distribution of the blood between the upper and lower parts of the body at increased intra-abdominal pressure, the total bloodflow to the heart will be considerably reduced. This reduction, which was up to 24 % of the initial value at an abdominal pressure of 36 cm water, easily explains the reduced blood pressure at that abdominal pressure.

CHAPTER IX

THE INFLUENCE OF INTRA-ABDOMINAL PRESSURE ON THE PORTAL BLOOD CIRCULATION AS SHOWN BY PORTAL ANGIOGRAPHY

Portal angiography, or portography, is a method used by many scientists for various purposes. Friedman, Frank, and Fine (1951) used this method for studying the portal circulation in dogs with haemorrhagic shock. They determined the size of the portal branches before and during the state of shock, and found that, while during shock the width of the branches was diminished in diameter, the use of dibenamin excluded this effect. They considered that the reduction in the width of the portal branches was caused by an active contraction of these branches.

Daniel and Prichard (1949, 1950, and 1951 a and b), using rats among other animals, studied the portal bloodflow through the liver by means of a rapid serial angiography during different experimental stages. They showed (1951 a) that during certain stages the portal blood flows only through the central parts of the liver and thus, owing to the shortened route, passes through the liver more quickly. Such shortened pathways exist between the bigger stems of the portal vein and the hepatic vein, but the portal blood always passes the sinusoids. While these two authors could not show any cause for this restricted trans-hepatic bloodflow, they assumed the existence of a neuro-vascular mechanism. In a later work (1951 b) they showed a constriction of the portal vessels produced by an electric stimulus of the hepatic nerves (plexus hepaticus). A restricted trans-hepatic circulation was not, however, always obtained by this procedure. They were able to effect similar angiograms by intra-portal injections of adrenalin, and in this case the effect was chiefly seen in the smaller vessels of the intra-hepatic portal venous tree.

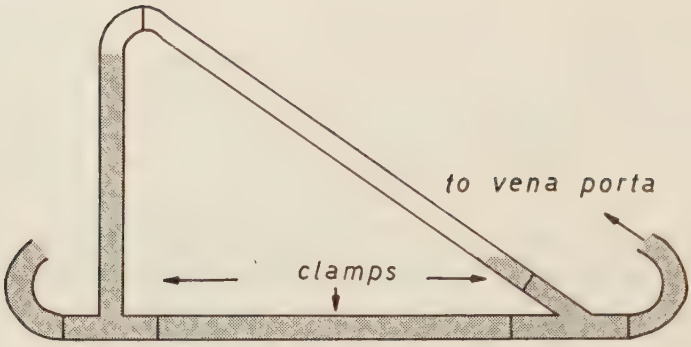


Fig. 26. Shunt arrangement for contrast infusion in portal vein. Shadowed area blood, white area contrast medium. During infusion of contrast medium horizontal tube is clamped.

Experimental Methods

For the experiment the animals were prepared as described in Chapter II, with a shunt connected between the common mesenteric vein and the portal vein (see page 23). The part of the shunt outside the animal consisted of two branches. One of these was formed like an angle, with one leg placed vertically. The arrangement of the shunt is shown in Fig. 26. In this way it was possible to let the blood pass through either the straight tube or the bent one. In the tilted leg of the shunt the contrast medium was placed independently of the portal bloodflow when the latter passed through the straight tube. When the blood was allowed to go through the bent tube, a contrast injection was obtained in the portal vein without any change of the pressure conditions in this vessel. The contrast tube was bent so as to make it possible to follow the contact surface between the blood and the contrast medium as it moved towards the liver. In this way the speed of the bloodflow could be judged and the right moment for exposure could thus be determined. The contrast medium used in these experiments was thorotrast, a colloidal preparation containing 25 % thorium-dioxide, 4 cc for each series of angiograms being sufficient to fill out the whole portal tree simultaneously. As the contrast medium filled out the whole length of the portal system traversed, streamline phenomena were eliminated, thus making it easier to estimate the width of the portal vessels and rendering photography necessary merely in a ventro-dorsal direction.

During the experiment air was blown into the intestines (see page

25) until the intra-abdominal pressure rose to between 30 and 40 cm water. The first angiogram of the portal vein was taken at normal intra-abdominal pressure, subsequent angiograms being taken at intervals as the intra-abdominal pressure was raised. The last exposure was made when the abdomen had been relieved of pressure by letting the air out of the intestines and reopening the abdomen.

All angiograms were taken in a ventro-dorsal projection, as stated, and the distance between the X-ray tube and the rabbit, as well as between the rabbit and the cassette, was always constant.

A series of three X-ray films was taken with each contrast injection, with a time interval of 1–4 seconds, depending on the speed of the portal bloodflow, the interval being increased as the intra-abdominal pressure rose. With the help of a simple cassette changer it was possible to insert the consecutive X-ray plates rapidly. The serial angiograms secured a complete picture of the portal venous tree, and comparison of the films showed when all the contrast medium was in the liver.

The time of exposure for each separate portogram varied between 0.15 and 0.20 seconds. The available X-ray apparatus did not allow of a shorter time of exposure.

Results, Deductions and Conclusions

The experiments include portograms on rabbits both under normal conditions and during increased intra-abdominal pressure. As the results are identical, an account will be given of only two angiograms. One of them shows the conditions in the portal system when the portal vein and the liver are subjected to high intra-abdominal pressure. The other shows the appearance when the liver and portal vein are freed from intra-abdominal pressure by means of a separating wall which screens off the upper part of the abdomen (see page 24).

The results are best seen in the X-ray series shown in Fig. 27, with the dates of the experiments indicated underneath. In judging the pictures, account has been taken of both the intra-hepatic portal branches and the extra-hepatic part of the portal vein. As judged by X-rays, the portal stem differs from the intra-hepatic portal vessels in that no small vessels appear to issue from it.

When the contrast medium is made to flow into the portal system, the bent leg of the shunt empties itself in about three seconds. When the intra-abdominal pressure is raised the rate of inflow of the

contrast medium is reduced. At an intra-abdominal pressure of about 30 cm water the contrast medium takes about 3–4 times as long to leave the shunt.

At normal intra-abdominal pressure the angiograms show a complete contrast picture of the whole portal tree. There will be no difficulties in following the portal branches far out into the periphery of the liver. As intra-abdominal pressure is raised, the filling of the portal tree with contrast medium deteriorates increasingly. The portal tree seems to contract, the outline of the liver and its vessels becomes less distinct, and the sharp appearance of the portal tree disappears. When the contrast medium reaches the sinusoids, the liver takes on a blurred appearance which in some cases makes it difficult to interpret the X-ray films. This appearance may be a sign of a very slow bloodflow through the liver.

When the intra-abdominal pressure is relieved, the portal tree fills with contrast medium almost to the same extent as it did before the intra-abdominal pressure was raised.

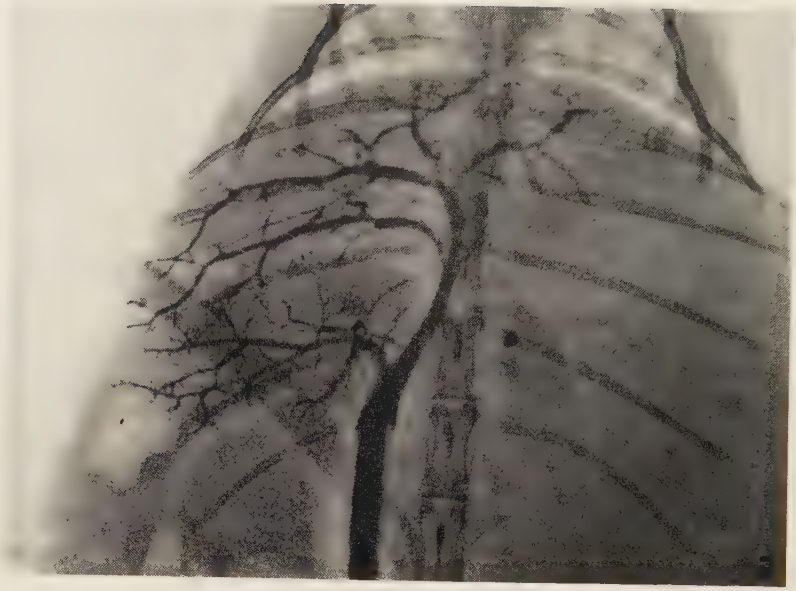
As regards the diameter of the extra-hepatic portion of the portal vein, it seems largely to depend on the degree of intra-abdominal pressure. In the experiment illustrated in Fig. 27 the diameter of the portal vein at an intra-abdominal pressure of 30 cm water is only one-third of the width it has when intra-abdominal pressure is normal.

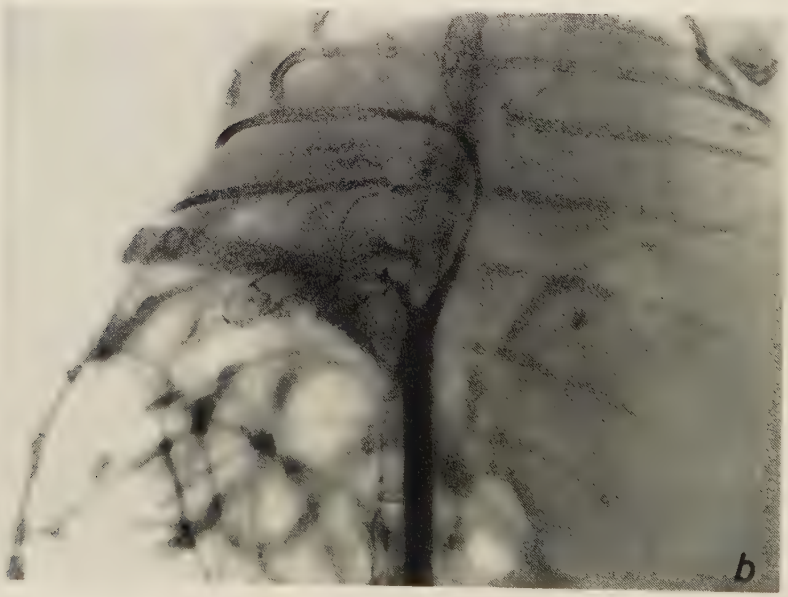
As the portal vein lies completely unprotected against the influence of the intra-abdominal pressure, its reduction in width is easily explained. During several of these angiographic experiments the portal pressure was higher than the intra-abdominal pressure, and in spite of this the angiograms showed a narrowed portal vein. This indicates that the difference between the portal pressure and the intra-abdominal pressure has a certain importance as regards the maintenance of the width of the vessel as well as of the portal circulation. Even the intra-hepatic portal branches diminish considerably in size with the rising intra-abdominal pressure, and the peripheral vessel branches in the liver do not fill with contrast medium which passes only the central and bigger portal branches. In other words, the portal bloodflow through the liver, and especially through the peripheral parts of it, seems to be dependent on the prevealing degree of intra-abdominal pressure, and to be considerably diminished when this pressure is high.

In the second experiment described in this chapter, the portal angiogram shows the portal vein and liver protected from the intra-abdominal pressure by a separating wall placed just below the liver. This has been done to eliminate the effect of the pressure on the portal blood circulation in the liver, and to exclude the possibility of a neuro-vascular reflex causing the diminution of the portal tree — i.e., to exclude an active vessel contraction which might possibly arise when the intestines are distended. (Compare the vasomotor reflexes shown on distension of the duodenum, Carmichael, Doupe, Harper, and McSwiney, 1939).

As Fig. 28 shows, no change is seen in the appearance of the vessel tree when the liver is protected from the intra-abdominal pressure caused by the distended intestines.

The result is that a high intra-abdominal pressure compresses the liver to such an extent that the bloodflow through it diminishes, especially in the peripheral parts of the liver.

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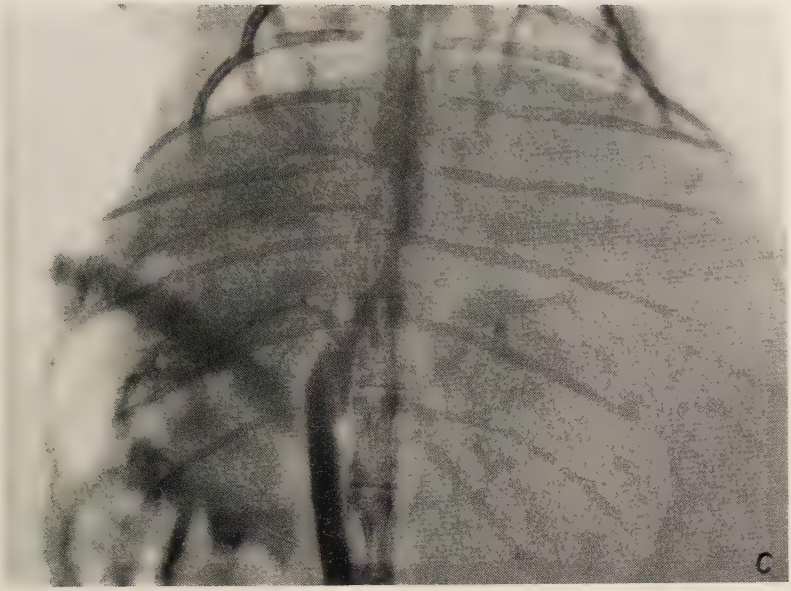
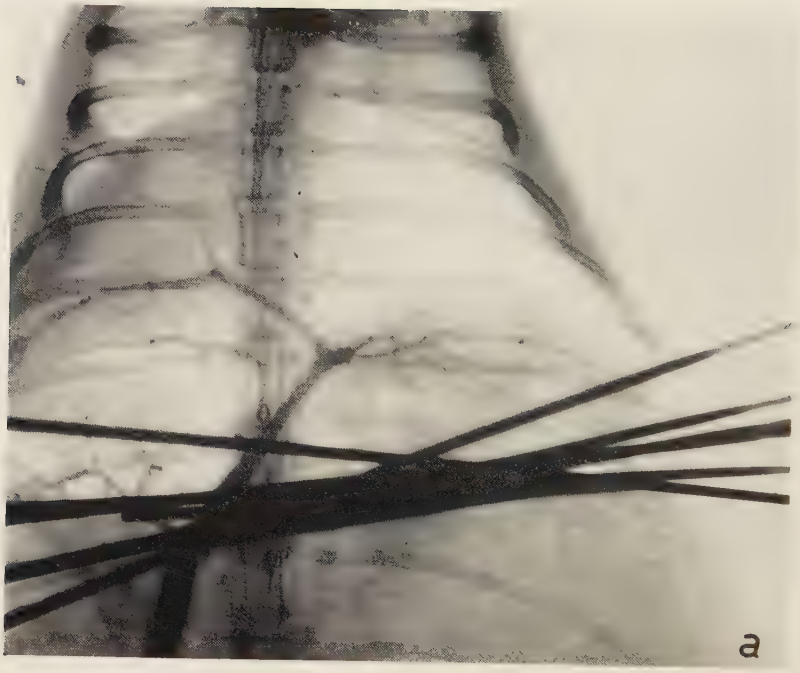


Fig. 27.

a) Portogram at normal intra-abdominal pressure. Portal pressure 19 cm water.

b) Portogram at an intra-abdominal pressure of 35 cm wasser. Portal pressure 34 cm water.

c) Portogram when abdominal pressure was relieved. Portal pressure 20 cm water.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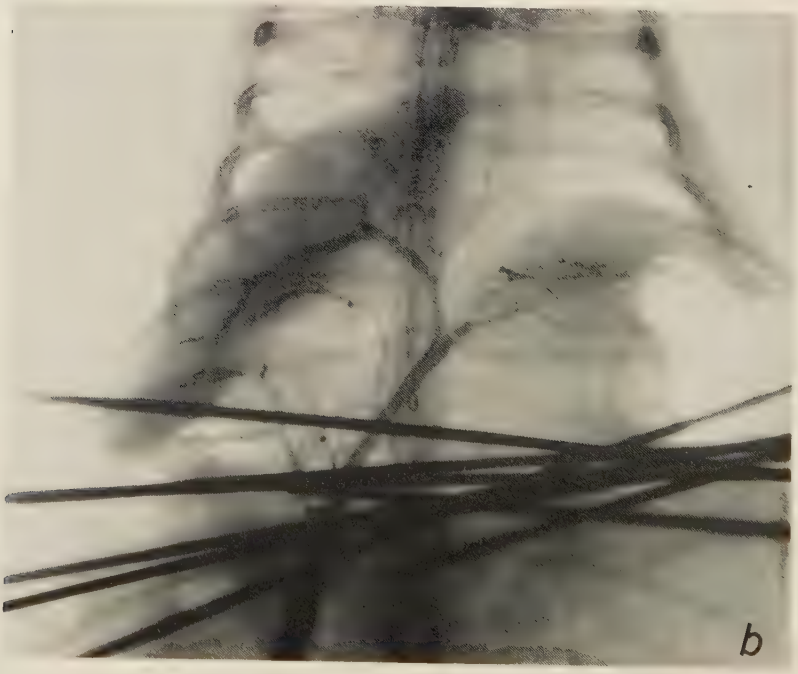
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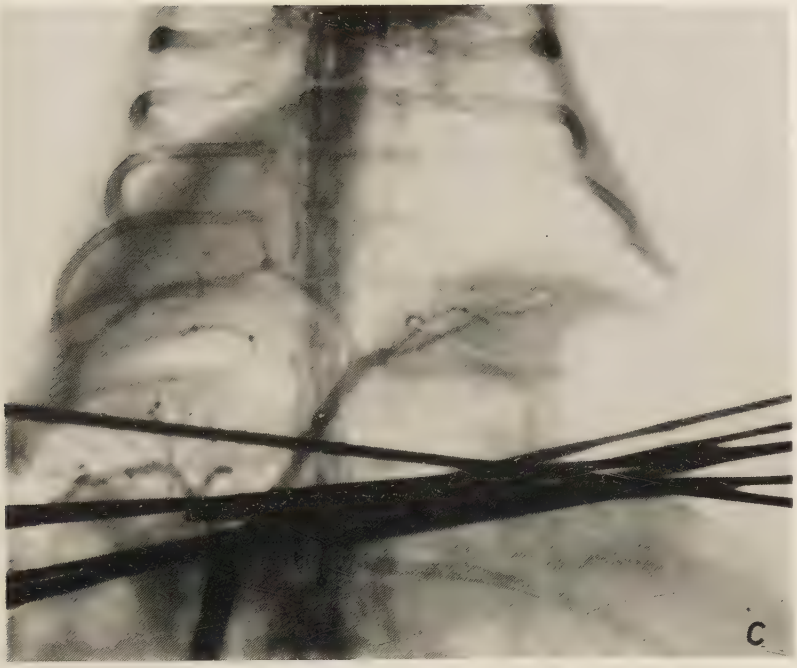

Fig. 28. Liver protected from pressure by knitting needle trellis.

a) Portogram at a normal intra-abdominal pressure.

b) Portogram at an intra-abdominal pressure of 34 cm water.

c) Portogram when abdominal pressure was relieved.

Fig. 29. Neoprene cast showing the portal tree of a liver at normal intra-abdominal pressure. Weight of rabbit 2.0 kg.

Fig. 30. Neoprene cast of the portal tree of a liver subjected to an intra-abdominal pressure of 35 cm water. Weight of rabbit 2.2 kg.

CHAPTER X

THE APPEARANCE OF THE PORTAL VENOUS TREE AT NORMAL AND INCREASED INTRA-ABDOMINAL PRESSURE

A Comparative Investigation with Neoprene Casts

In accordance with several investigations presented in this study, intra-abdominal pressure seems to compress the liver to a certain extent. The pliability of the liver under pressure probably affects its blood vessels in the first place. If these vessels are reduced in their cross-section, the flow through the organ is rendered more difficult. In addition to the reduced flow through the organ there is also seen an increased portal pressure.

The studies of the portal system during increased intra-abdominal pressure, as shown by angiograms, definitely suggest a considerably diminished portal tree, and with it a decreased cross-section of the vessels in the liver.

In order to obtain further proof of the diminished cross-section of the vessels in the liver, I have made casts of the portal tree in living rabbits during normal intra-abdominal pressure and during an increased pressure of 30–35 cm water.

Method:

For the casts I have used neoprene latex 571. This is a milk-like suspension consisting of rubber particles and containing 59 % solid components. These particles are smaller than blood corpuscles and have a size of about 1–2 μ. The neoprene is quickly polymerized — within a few minutes in the smaller vessels. The process is initiated in the presence of ions, and has a quicker course the more polyvalent the ions.

This method in the study of vessels which I have used in these experiments, was first employed by Lieb (1940) and has become familiar through the work of Trueta et al. (1947).

The rabbits were prepared in the usual way with a by-pass tube connection between the common mesenteric vein and the portal vein. The neoprene suspension was injected with the help of a pressure flask in a branch of the by-pass tube after the blood from the intestines had been arrested. The injection pressure used was the same as the prevailing pressure in the portal vein. In a few cases, during high intra-abdominal pressure when the portal pressure was too slow, the neoprene was injected with a pressure 5–10 cm water higher than the prevailing portal pressure.

After a neoprene injection the animals died within a few minutes, but they remained untouched on the operating table for a few hours afterwards in order to give the neoprene time to set even in the biggest vessels. The liver was then taken out of the animal and placed in a warm solution of concentrated hydrochloric acid in order to macerate it, and the preparation was then ready.

Results:

The casts of the portal tree during normal and increased intra-abdominal pressure are illustrated in Figs. 29 and 30. The difference between the two casts is very marked and shows a considerably diminished portal vascularity of the liver caused by the pressure to which the liver was subjected.

In the casts of the portal tree during normal pressure even very small vessels can be seen. There are a great many of these and they give the preparation a cauliflower-like appearance. The larger portal venous stems are round and well-formed.

The appearance of the casts during a pressure of 30–35 cm water shows that there are exceedingly few of the small portal vessels present. The larger portal vessels are compressed and thin. The preparation has a fragile appearance in comparison with the other, and reminds one of a tree stripped of its leaves.

A possible source of error with this method is the fact that the neoprene settles before it reaches the smaller vessels, and even plugs some of the large vessels. This risk is greater during a high intra-abdominal pressure when the portal bloodflow is reduced. In order to exclude this source of error I have, before injecting the neoprene, rinsed through the portal system with distilled water in order to flush away the blood. The casts made in this way barely differed from the rest.

Summary:

The appearance of the portal tree during normal and increased intra-abdominal pressure has been studied with the help of neoprene casts on living rabbits. There was a considerable difference in the appearance of the portal tree, resulting from a reduced portal vascularity in the liver and an impaired portal bloodflow through it. The results also show indirectly that a liver subjected to a pressure of up to 35 cm water is compressible.

SUMMARY

The present work is an investigation of the effect of increased intra-abdominal pressure on the liver and its blood-provision over the portal vein.

The investigation is purely experimental and contains experiments on rabbits. The increased intra-abdominal pressure was developed by blowing air into the intestines in order to produce such conditions as are prevailing during ileus and post-operative meteorism.

The size of the portal flow under different conditions was determined by a new type of flowmeter which was connected between the common mesenteric vein and the portal vein. The spleenic vein was always tied off. The flowmeter allows an absolute determination of the blood-volume per time unit.

In the first place the size of the bile flow in relation to the blood pressure and the portal flow has been studied. As regards the first-mentioned relationship, the preservation of the blood pressure seems to be of importance for the maintenance of the size of the bile secretion, which suggests a filtration as a component in the mechanism of bile production. There seems to be no relationship between the size of the portal flow and the size of the bile secretion. If the blood pressure is maintained there is no reduction in the bile secretion even if the whole portal flow is led past the liver. The provision of blood to the liver over the hepatic artery seems to be sufficient for the maintenance of bile secretion. (Chapter III.)

The arterial blood pressure in relation to intra-abdominal pressure has also been studied. An increased blood pressure was obtained in most cases when intra-abdominal pressure was raised. Possible reasons for this are discussed. The size of the bile flow was practically unchanged at intra-abdominal pressures of up to 20–25 cm water, when a powerful reduction appeared. This reduction is due to the fact that the liver is exposed to a pressure that is higher than the bile secretion pressure, that is, a pressure against which the liver can no longer produce bile. If the liver is protected from the influence of

intra-abdominal pressure, bile secretion is relatively unchanged in relation to intra-abdominal pressure. (Chapter IV.)

With an increase of the intra-abdominal pressure there is an increase in the pressure of the veins of the abdomen. This pressure is somewhat higher than the intra-abdominal pressure. In this way, part of the circulation through the abdomen is maintained in spite of the rising intra-abdominal pressure. Pressure is maintained in the veins by the arterial blood pressure, which is transferred over the capillaries or arteriovenous shunts. Even the intra-hepatic venous pressure — the pressure in the branches of the portal vein and the hepatic vein — increases in relation to intra-abdominal pressure. (Chapter V.)

Increased intra-abdominal pressure due to distended intestines renders more difficult both the bleeding through the intestinal wall and the blood circulation in the whole portal system. The reduction of the portal blood flow during increased intra-abdominal pressure is considerable. At an abdominal pressure of between 25 and 39 cm water the portal blood flow was reduced by 70–93%, i.e. 30–7% of its initial value. A major part of the increased resistance met by the portal blood flow originates from the liver when this organ is subjected to pressure. If the liver is protected from pressure, intra-abdominal pressure does not reduce the portal bloodflow so much as it would have done otherwise. (Chapter VI.)

A *relative* determination has been made of the oxygen saturation of the portal blood in relation to intestinal distention and thereby increased intra-abdominal pressure. In about half of these experiments there was an increase in the oxygen saturation of up to 70% at an abdominal pressure of 15–25 cm water. At a higher abdominal pressure the oxygen saturation was quickly reduced and fell below the initial value. The presence of arteriovenous shunts in the intestinal wall may possibly account for this phenomenon. In other experiments again there was no increase in the oxygen saturation of the portal blood. The arteriovenous shunts seem to open under certain and so far unknown conditions during intestinal distention. (Chapter VII.)

The importance of intra-abdominal pressure for the total bloodflow from the body below the diaphragm was determined in experiments where the blood flow was measured in the inferior caval vein above the diaphragm. At an abdominal pressure where the portal

flow was reduced by about 80% there was a reduction in the blood flow of the inferior caval vein by only 37%. The blood flow in the splanchnicus area seems to decline to a considerably higher degree than does the remaining circulation below the diaphragm at the same pressure. It is probable that the reduced portal blood flow is to some extent compensated over other capillary systems. (Chapter VIII.)

The portal vein and its branches in the liver were studied with the help of angiograms during normal and increased intra-abdominal pressure. The size of the portal tree was considerably reduced at abdominal pressures over 30 cm water. The circulation through the superficial layers of the liver ceased almost completely, and the portal branches decreased about $^2/_3$ in width. The reason is the effect of abdominal pressure on the liver. This experiment shows that a liver is compressible and that the capacity of the liver vessels is to a great extent dependent on the pressure to which it is subjected. (Chapter IX.)

With neoprene casts of the liver done *in vivo* at normal and increased intra-abdominal pressure it has been possible to obtain a more objective proof of the dependence of the liver circulation upon abdominal pressure. The casts made at normal abdominal pressure show that even very small vessels are well filled. On the casts made at a pressure of over 30 cm water the smallest portal vessel branches are missing, and the bigger branches are flattened and thin. An increased intra-abdominal pressure causes a demonstrable reduction of the vessel pathways — cross section of the vessels — in the liver. (Chapter X.)

Judging by the above-mentioned results an increased intra-abdominal pressure, caused by distension of intestines, seems to reduce the portal bloodflow in an extremely high degree. The cause of the reduced bloodflow seems to be a purely mechanical effect of the increased abdominal pressure. Therefore, it is quite probable that during ileus, when there is an increased intra-abdominal pressure, the portal bloodflow is reduced; in other words, the blood supply to the liver is reduced.

RÉSUMÉ

Ce travail comporte un examen de l'effet de la pression surélevée intraabdominale sur le foie et de l'arrivée du sang dans le foie par la veine porte.

Les recherches effectuées ici sont d'ordre purement expérimental et sont tentées sur des lapins. Une pression intraabdominale surélevée a été provoquée en soufflant de l'air dans les intestins afin d'obtenir les mêmes conditions que dans certaines formes d'iléus et de météorisme postopératoire.

L'importance du flux du sang dans la veine porte a été déterminée dans différents cas, par un nouveau type de «Stromuhr» que l'on a attaché entre la vena mesenterica communis et la vena portae. La veine de la rate a été ligaturée. Le Stromuhr permet de déterminer exactement la quantité de sang qui y passe par unité de temps.

On a examiné en premier lieu l'importance de l'écoulement de la bile par rapport à la tension artérielle et au flux de sang dans la veine porte. En ce qui concerne la première de ces deux relations le maintien d'une tension égale semble être d'une grande importance pour maintenir le volume de la sécrétion biliaire, ce qui semble indiquer que la filtration est une composante du mécanisme de formation de la bile. Il ne semble pas y avoir de relation entre l'ampleur du flux de sang dans la veine porte et l'ampleur de la sécrétion de la bile. Si on maintient une tension égale il ne se produit aucune diminution de la sécrétion de la bile même si tout le sang de la veine porte est détourné du foie. Le sang amené au foie par l'artère hépatique est ainsi suffisant pour maintenir la sécrétion de la bile. (Chap. III.)

On a examiné la relation entre la tension artérielle et la tension intraabdominale. On a obtenu dans plusieurs cas une augmentation de la tension lorsque la pression intraabdominale augmentait. Les raisons de ce phénomène sont discutées. L'importance de l'écoulement de la bile est restée à peu près la même pour une pression intraabdominale allant jusqu'à 20—35 cm d'eau, limite à laquelle une forte diminution se fait sentir. Cette diminution provient de ce que le

foie est soumis à une pression qui dépasse la pression de la sécrétion de la bile, c. a. d. une pression empêchant les cellules du foie de continuer à produire de la bile. Si l'on empêche la pression intraabdominale d'exercer son action sur le foie, la sécrétion de la bile reste à peu pres la même par rapport à la pression intraabdominale. (Chap. IV.)

En même temps que la pression intraabdominale augmente on observe aussi un augmentation de la pression dans les veines de l'abdomen, dont la pression se maintient un peu au-dessus de la pression intraabdominale. De cette sorte on entretient toujours une certaine circulation dans l'abdomen malgré l'augmentation de la pression intraabdominale. La pression dans les veines est maintenue par la tension artérielle, laquelle est transmise par voies capillaires ou par shunts *artérioveineux*. Même la pression dans les vaisseaux intrahépatiques, et dans les ramifications de la veine porte et de la veine hépatique augmente par rapport à la pression intraabdominale. (Chap. V.)

Une pression intraabdominale surélevée provoquée par des intestins distendus complique d'une part l'écoulement du sang des parois de l'intestin et d'autre part la circulation dans tous le système porte. La diminution du flux de sang dans la veine porte lors de l'élévation de la pression intraabdominale est considérable. Pour une pression abdominale de 25—30 cm d'eau le flux de sang de la veine porte est réduit de 70—93% c. a. d. de 30—7% par rapport à la valeur normale. Une grande partie de la résistance accrue du flux de sang de la veine porte se produit dans le foie lorsque celui-ci subit une pression. Lorsque le foie n'est plus soumis à la pression intraabdominale le flux de sang de la veine porte ne diminue pas dans les mêmes proportions sous l'effet de la pression intraabdominale surélevée ce qui autrement est le cas. (Chap. VI.)

On a déterminé la saturation du sang de la veine porte en oxygène par rapport à la distension des intestins et à la pression intraabdominale accrue qui en résulte. Dans environ la moitié de ces investigations on a abtenu pour une pression abdominale de 15 à 25 cm d'eau une augmentation de la saturation en oxygène allant jusqu'à 70%. Pour une pression abdominale plus élevée la saturation en oxygène a rapidement diminué et se trouve ainsi en dessous de la valeur initiale. La présence de shunts artérioveineux dans les intestins peut expliquer ce phénomène. Au cours d'autres expériences on n'a pas obtenu d'augmentation de la saturation en oxygène du sang de la veine

porte. Les shunts artérioveineux semblent pour cette raison s'ouvrir, au moment de la distension des intestins, sous l'effet de certaines conditions actuellement inconnues. (Chap. VII.)

L'importance de la pression intraabdominale pour toute la partie du système sanguin situé sous le diphragme, a été déterminée par l'expérience au cours de laquelle on a mesuré le flux du sang dans la veine cave inférieure au-dessus du diaphragme. Pour une pression abdominale provoquant une diminution du flux de la veine porte d'environ 80 % on obtient une diminution du flux de la veine cave de seulement 37 %. Le flux de sang de la région splanchnique doit donc pour une même pression abdominale diminuer de façon beaucoup plus prononcée que le reste de la circulation dans l'abdomen. Il est probable que le flux de sang réduit de la veine porte est en une certaine mesure compensé dans d'autres vaisseaux sanguins. (Chap. VIII.)

La veine porte et ses ramifications dans le foie sont étudiées, à l'aide *d'angiographes*, pour une pression intraabdominale normale et pour une pression surélevée. La grandeur de l'arbre porte diminue considérablement pour une pression abdominale de plus de 30 cm d'eau. Outre que la circulation du sang dans les couches superficielles du foie cesse presque entièrement les ramifications plus importantes de la veine porte réduisent leur largeur des 2/3 environ. Ceci dépend uniquement de la pression de l'abdomen contre le foie. Cet examen montre également que le foie est relativement facilement comprimable et que le volume de sa *vascularité* dépend de la pression exercée sur elle. (Chap. IX.)

Avec des moulages en *neoprène* de l'arbre porte exécutés in vivo, pour une pression intraabdominale normale et pour une pression surélevée, on a obtenu une preuve plus objective de ce que la circulation du foie dépend de la pression intraabdominale. Les moulages exécutés pour une pression abdominale normale ont montré un bon remplissage des vaisseaux et même des très petits vaisseaux. Les moulages, pour une pression abdominale de plus de 30 cm d'eau, manquaient des petites ramifications de la veine porte. Les grandes ramifications de la veine porte étaient minces et aplaties. Une pression intraabdominale surélevée entraîne ainsi une diminution apparente du volume des vaisseaux et des coupes transversales dans le foie. (Chap. X.)

A en juger d'après le résultat obtenu ci-dessus une tension intra-abdominale surélevée, provoquée par distension des intestins, réduit

de façon très sensible le flux de sang dans la veine porte. La raison de cette diminution du flux de sang semble être un effet purement mécanique de la pression abdominale augmentée. C'est pourquoi il est très probable que, pour les iléus s'accompagnant d'une pression intraabdominale surélevée, il faille envisager un flux de sang moins important dans la veine porte, en d'autres termes un apport réduit de sang au foie.

ZUSAMMENFASSUNG

Die vorliegende Arbeit umfasst eine Untersuchung der Einwirkung des erhöhten intraabdominalen Druckes auf die Leber und deren Blutversorgung über die Vena Porta.

Die Untersuchungen sind rein experimentell und umfassen Versuche an Kaninchen. Erhöhten intraabdominalen Druck erzielte man durch Lufteinblasung in die Därme in der Absicht, Verhältnisse zu schaffen, die gewissen Formen von Ileus und postoperativem Meteorismus entsprechen.

Die Grösse der Portadurchströmung unter unterschiedlichen Verhältnissen wurde mit einer Stromuhr neuen Typs bestimmt, welche zwischen Vena mesenterica und Vena Porta eingekoppelt wurde. Die Milzvene wurde ligiert. Die Stromuhr gestattet eine absolute Bestimmung der Blutmenge, die in der Zeiteinheit durch sie fliesst.

Als erstes wurde die Grösse des Gallflusses in Verhältnis zu Blutdruck und Portadurchströmung untersucht. Was die erste Relation anbetrifft, so scheint die Aufrechterhaltung des Blutdruckes von grosser Bedeutung für die Einhaltung der Grösse der Gallesekretion zu sein, welches dafür spricht, dass Filtration eine Komponente im Mechanismus der Gallebildung ist. Relationen zwischen der Grösse der Portadurchströmung und der Grösse der Gallesekretion scheinen nicht vorzuliegen. Bei Einhaltung des Blutdruckes kommt es zu keiner Minderung der Gallesekretion, sogar dann nicht, wenn man den gesamten Portablutstrom an der Leber vorbeileitet. Die Blutversorgung der Leber über die Arteria hepatica ist somit ausreichend für die Aufrechterhaltung der Gallesekretion. (Kap. III.)

Das Verhalten des arteriellen Blutdruckes gegenüber intraabdominalem Druck wurde untersucht. Eine Blutdrucksteigerung erhielt man in verschiedenen Fällen bei Erhöhung des intraabdominalen Druckes. Die Ursachen hierfür werden diskutiert. Die Grösse des Gallflusses hielt sich ziemlich unverändert bei intraabdominalem Druck bis 20–25 cm Wasser, dann machte sich eine kräftige Verminderung geltend. Diese Verminderung beruht darauf, dass die

Leber einem Druck ausgesetzt wird, der den Gallesekretionsdruck übersteigt, d. h. den Druck gegen den die Leberzelle nicht mehr länger Galle produzieren kann. Verhindert man den intraabdominalen Druck, seine Wirkung auf die Leber auszuüben, so verbleibt die Gallesekretion ziemlich unverändert gegenüber dem intraabdominalen Druck. (Kap. IV.)

Bei einer Steigerung des intraabdominalen Druckes kommt es ebenfalls zu einer Steigerung des Druckes in den Bauchvenen, deren Druck sich etwas über dem intraabdominalen Druck hält. Auf diese Weise wird immer eine gewisse Zirkulation in den Bauchgefässen aufrechterhalten, trotz Steigerung des intraabdominalen Druckes. Der Druck in den Venen wird durch den arteriellen Blutdruck aufrechterhalten, der via Kapillaren oder arteriovenöse shunts mitgeteilt wird. Sogar der intrahepatische Gefässdruck, d. h. der Druck in den Zweigen der Vena Porta und der Vena hepatica erhöht sich im Verhältnis zum intraabdominalen Druck. (Kap. V.)

Bei einem erhöhten intraabdominalen Druck — hervorgerufen durch erweiterte Darmschlingen — wird einerseits die Durchblutung der Darmwände und andererseits die Zirkulation im gesamten Portasystem erschwert. Die Verminderung der Portadurchströmung bei erhöhtem intraabdominalen Druck ist bedeutend. Bei einem intraabdominalen Druck zwischen 25–39 cm Wasser wird die Portadurchströmung um 70–93 % vermindert, d. h. auf 30–7 % der normalen Grösse der Portadurchströmung. Ein grosser Teil des erhöhten Widerstandes für den Portablutstrom entsteht in der Leber, wenn diese dem Druck ausgesetzt wird. Wird die Leber druckentlastet, so ist die Verminderung der Portadurchströmung geringer als es sonst bei Steigerung des intraabdominalen Druckes der Fall ist. (Kap. VI.)

Eine *relative* Bestimmung der Sauerstoffsättigung der Portablutes im Verhältnis zur Darmerweiterung und damit zum erhöhten intraabdominalen Druck wurde ausgeführt. In ungefähr der Hälfte dieser Untersuchungen fand man eine Erhöhung der Sauerstoffsättigung bei intraabdominalem Druck von 15–25 cm Wasser bis zu 70 %. Bei höherem intraabdominalen Druck verminderte sich die Sauerstoffsättigung schnell und unterschritt damit den Ausgangswert. Vorkommen von arteriovenösen shunts in der Darmwand können dieses Phänomen erklären. Bei anderen Experimenten wiederum erhielt man keine Erhöhung der Sauerstoffsättigung des Portablutes. Die

arteriovenösen shunts scheinen sich also bei Darmdistension unter gewissen, bisher unbekannten Bedingungen zu öffnen. (Kap. VII.)

Es wurde die Bedeutung des intraabdominalen Druckes für den gesamten Blutrückfluss von den unterhalb des Diaphragma gelegenen Körperpartien untersucht, indem man die Blutmenge in der Vena cava inf. oberhalb des Diaphragma bestimmte. Bei einem intraabdominalen Druck, bei welchem die Portadurchströmung um ungefähr 80% vermindert wurde, erhielt man eine Verminderung der Cavadurchströmung um nur 37%. Bei gleichem intraabdominalen Druck dürfte sich also im Splanchnicusgebiet die Blutdurchströmung in bedeutend stärkerem Maasse vermindern als die übrige Zirkulation unterhalb des Diaphragma. Es ist anzunehmen, dass die reduzierte Portadurchströmung in irgendeiner Form über andere Gefässgebiete kompensiert wird. (Kap. VIII.)

Die Vena Porta und ihre Zweige wurden mit Hilfe von Angiographien bei normalem und erhöhtem intraabdominalen Druck untersucht.

Die Grösse der Portaverzweigungen verminderte sich bedeutend bei intraabdominalem Druck von über 30 cm Wasser. Die Durchblutung der äusseren Schichten der Leber hörte fast vollständig auf und die Weite der grösseren Portazweige verminderte sich um ca. $^2/_3$. Dieser Effekt beruht nur auf der Kompression der Leber durch den Bauchdruck. Diese Untersuchungen zeigen auch, dass die Leber verhältnismässig leicht kompressibel ist und dass die Weite der Lebergefässe in hohem Grade abhängig ist von dem Druck der gegen sie ausgeübt wird. (Kap. IX.)

Mit Neopreneausgiessungen der Portaverzweigungen, ausgeführt *in vivo* bei normalem und erhöhtem intraabdominalen Druck erhielt man einen objektiveren Beleg für die Abhängigkeit der Leberzirkulation vom intraabdominalen Druck. Bei normalem Bauchdruck gemachte Ausgiessungen zeigen eine gute Gefässfüllung bis in die kleinsten Äste. Bei einem intraabdominalen Druck von über 30 cm Wasser fehlen die kleinsten Portazweige in den Ausgiessungen. Die grösseren Portazweige sind abgeplattet und dünn. Ein erhöhter intraabdominaler Druck führt also eine beweisbare Verminderung der Gefässbahnen — des Gefässquerschnittes — in der Leber mit sich. (Kap. X.)

Nach den obenstehenden Resultaten zu urteilen scheint ein erhöhter intraabdominaler Druck — erzeugt durch Darmdistension — die

Portadurchströmung in ausserordentlich hohem Grad zu reduzieren. Die Ursache für die verminderte Blutdurchströmung scheint ein rein mechanischer Effekt des erhöhten Bauchdruckes zu sein. Es ist deswegen sehr wahrscheinlich, dass man bei Ileuserkrankungen, bei denen erhöhter intraabdominaler Druck vorkommt, mit einer verminderten Portadurchströmung zu rechnen hat; mit anderen Worten mit einer herabgesetzten Blutversorgung der Leber.

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